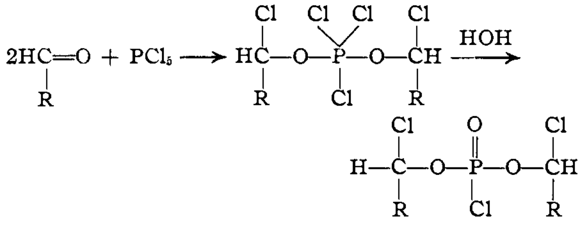
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

# The Action of Phosphorus Pentachloride upon *aldehydo*-Galactose Pentaacetate. The 1,1-Dichloride of *aldehydo*-Galactose Pentaacetate

BY M. L. WOLFROM AND D. I. WEISBLAT

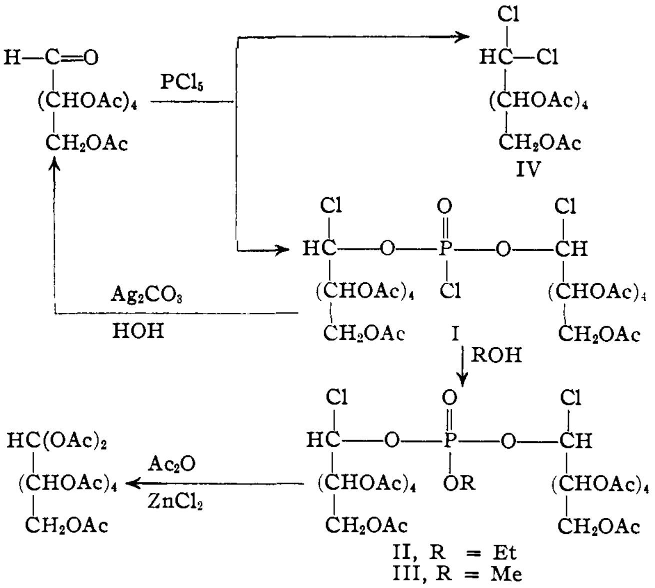
The action of phosphorus pentachloride upon aldehydes to produce the 1,1-dichlorides[1] is a well-known reaction. We were interested in its extension to an *aldehydo*-sugar acetate and were successful in obtaining a crystalline product in the galactose structure. The product, 1,1-dichloro-*aldehydo*-*d*-galactose pentaacetate (IV) is the first substance of this type in the sugar series. It is a very stable substance and reduces Fehling solution only on prolonged boiling. It does not reduce neutral copper acetate solution on boiling. We have found that the reduction of neutral copper acetate solution is a general property of *aldehydo*-sugar acetates and also of the very reactive acetyl chloride carbonyl addition compound of *aldehydo*-galactose pentaacetate.[2] The behavior of a number of significant sugar structures toward this reagent is tabulated in Table I. We believe that this lack of reduction toward neutral copper acetate confirms our assigned structure for substance IV.

If the reaction of phosphorus pentachloride with *aldehydo*-galactose pentaacetate is carried out in ether solution, an insoluble reaction product separates which is assigned structure I. This may be considered as a carbonyl addition compound of phosphorus pentachloride with two moles of the aldehyde in which two of the chlorine atoms attached to phosphorus have been hydrolyzed.



$$2\,\underset{\text{R}}{\text{HC}}{=}\text{O} + \text{PCl}_5 \longrightarrow \text{H}\overset{\text{Cl}}{\underset{\text{R}}{\text{C}}}\text{—O—}\overset{\text{Cl Cl}}{\underset{\text{Cl}}{\text{P}}}\text{—O—}\overset{\text{Cl}}{\underset{\text{R}}{\text{C}}}\text{H} \xrightarrow{\text{HOH}} \text{H—}\overset{\text{Cl}}{\underset{\text{R}}{\text{C}}}\text{—O—}\overset{\text{O}}{\underset{\text{Cl}}{\text{P}}}\text{—O—}\overset{\text{Cl}}{\underset{\text{R}}{\text{C}}}\text{H}$$

The structure of substance I, designated di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) chlorophosphate, is made probable by its analysis, its hydrolysis with water and silver carbonate to *aldehydo*-galactose pentaacetate and by the fact that it contains one reactive chlorine extremely readily replaceable by an alkoxyl group. On recrystallization from ethanol, I yields the substance II, designated di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) ethyl phosphate. II exhibits the predicted molecular weight and on acetylation with acetic anhydride and zinc chloride, yields *aldehydo*-galactose heptaacetate. The compound III, analogous to II but containing a methoxyl group, also was synthesized.



It is probable that the substance I represents a general structure for the initial reaction stages of aldehydes with phosphorus pentachloride. In the cyclic sugar structures, Freudenberg and Braun[3] have reported a crystalline reaction product of 2,3,6-trimethylglucose with phosphorus pentachloride which on analysis proved to be $(C_6H_8O_3(OCH_3)_3)_2PCl_3$. Helferich and du Mont[4] have obtained a crystalline tri-(β-*d*-glucopyranose tetraacetate)-6-phosphate by the reaction of phosphorus oxychloride with β-*d*-glucose 1,2,3,4-tetraacetate.

## Experimental

**Di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) Chlorophosphate (I).**—*aldehydo*-*d*-Galactose pentaacetate[5] (10 g.,

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[1] C. Friedel (A. Wurtz), *Compt. rend.*, **46**, 1015 (1857); A. Wurtz and C. Frapolli, *ibid.*, **47**, 418 (1858); A. Geuther, *Ann.*, **106**, 321 (1858).

[2] M. L. Wolfrom, THIS JOURNAL, **57**, 2498 (1935).

[3] K. Freudenberg and E. Braun, *Ann.*, **460**, 303 (1928).

[4] B. Helferich and H. du Mont, *Z. physiol. Chem.*, **181**, 300 (1929).

[5] M. L. Wolfrom, THIS JOURNAL, **52**, 2464 (1930).

TABLE I

REDUCTION OF *d*-GALACTOSE DERIVATIVES BY COPPER ACETATE[a]

| Substance | Time at b. p., sec.[b] | Reduction |
|---|---|---|
| *d*-Galactose | 0 | + |
| *β-d*-Galactopyranose pentaacetate | 120 | − |
| *α-d*-Galactopyranose pentaacetate | 120 | − |
| *aldehydo-d*-Galactose pentaacetate | 15 | + |
| *aldehydo-d*-Galactose isopropyl hemiacetal | 45 | + |
| *d*-Galactose heptaacetate | 50 | + |
| 1-Chloro-*d*-galactose hexaacetate | 60 | + |
| 1-Methoxy-*d*-galactose hexaacetate | 90 | + |
| 1-Chloro-1-ethoxy-*d*-galactose pentaacetate | 30 | + |
| *d*-Galactopyranose tetraacetate | 90 | + |
| 1,1-Dichloro-*aldehydo-d*-galactose pentaacetate[c] | 120 | − |
| Di-(1-chloro-*aldehydo-d*-galactose pentaacetate) chlorophosphate[c] | 120 | − |

[a] One mole equivalent of 0.05 g. *d*-galactose in 5 cc. of saturated aqueous cupric acetate solution. [b] In the case of a positive reduction, the time of boiling recorded is that at which visible reduction was initiated. *d*-Galactose gave a visible reduction before the boiling point was attained. [c] No reduction also on addition of ethanol.

1 mol) and powdered phosphorus pentachloride (5 g., 0.9 mol) were suspended in 200 cc. of anhydrous ether and refluxed for twelve hours in an all-glass apparatus equipped with a drying tube. The product began to separate from the reaction mixture within the first hour of reflux. At the end of this period of refluxing an equal volume of petroleum ether (b. p. 65–110°) was added and the mixture kept overnight at icebox temperature. The product was removed by filtration and washed three to four times with ether–petroleum ether (1:1); yield 4.5–6 g., m. p. 145–155°. The product was immediately recrystallized from about 80 parts of hot ethyl acetate; yield 3.5 g., m. p. 190° (dec.), spec. rot. −20° (26°; *c*, 2.2; $CHCl_3$).[6]

The substance was very soluble in chloroform, moderately so in acetone and practically insoluble in ether, petroleum ether and cold water. It showed no reduction toward copper acetate (see Table I) but slowly reduced boiling Fehling solution. It gave a positive Schiff test very slowly on standing. The material is very unstable unless of maximum purity, in which condition a sample in a desiccator over soda lime has shown no decomposition over a period of one year.

The substance was also formed by shaking the reaction mixture at room temperature over a period of several days. No appreciable difference was noted on starting with the aldehydrol form of *aldehydo-d*-galactose pentaacetate.

By working up the mother liquor material from the ethyl acetate recrystallizations by means of alcohol–water, a very small amount of 1,1-dichloro-*aldehydo-d*-galactose pentaacetate (see below) could be obtained in very high purity. No conditions could be found for converting compound I into the dichloride (IV).

*Anal.* Calcd. for $C_{32}H_{42}O_{23}Cl_3P$: Cl, 11.41; P, 3.32; saponification value (15 equivalents), 16.1 cc. 0.1 *N* NaOH per 100 mg. Found: Cl, 11.3; P, 3.34; saponification value (Kunz and Hudson procedure[7]), 16.0 cc.

**Hydrolysis of Di-(1-chloro-*aldehydo-d*-galactose pentaacetate) Chlorophosphate (I) to *aldehydo-d*-Galactose Pentaacetate.**—I (2 g.) was suspended in 100 cc. of toluene and 4 g. of freshly prepared silver carbonate and 0.5 cc. of water added. The mixture was refluxed for twenty-one hours with vigorous mechanical stirring. The silver salts were then removed by filtration and crystalline material was obtained by solvent removal under reduced pressure. The crystalline material was recrystallized from absolute ethanol and 0.3 g. of pure *aldehydo-d*-galactose pentaacetate ethyl hemiacetal was obtained which was identified by melting point (133–135°), mixed melting point and optical behavior in chloroform solution.[8]

**Di-(1-chloro-*aldehydo-d*-galactose pentaacetate) Ethyl Phosphate (II).**—When di-(1-chloro-*aldehydo-d*-galactose pentaacetate) chlorophosphate (I) was recrystallized from 75 parts of boiling absolute ethanol, hydrogen chloride was evolved and on cooling, filtering, and concentrating the mother liquors, a practically quantitative yield of the di-(1-chloro-*aldehydo-d*-galactose pentaacetate) ethyl phosphate (II) was obtained; m. p. 156–158°, spec. rot. −24° (21°; *c*, 1.3; $CHCl_3$).

The product was similar to substance I in solubility and behavior toward copper acetate, Fehling solution and the Schiff reagent.

*Anal.* Calcd. for $C_{32}H_{44}O_{23}(OC_2H_5)Cl_2P$: Cl, 7.53; P, 3.29; $OC_2H_5$, 4.79; saponification value (15 equivalents), 15.9 cc. of 0.1 *N* NaOH per 100 mg.; mol. wt., 941.6. Found: Cl, 7.60; P, 3.30; $OC_2H_5$, 5.0; saponification value,[7] 15.9 cc.; mol. wt. (Rast), 950.

**Conversion of Di-(1-chloro-*aldehydo-d*-galactose pentaacetate) Ethyl Phosphate (II) to *aldehydo-d*-Galactose Heptaacetate.**—II (1 g.) was dissolved in a solution of 0.3 g. of freshly fused zinc chloride in 10 cc. of acetic anhydride and the solution heated for one hour at 98°. The black solution was poured on a mixture of sodium bicarbonate and crushed ice. This mixture was extracted with chloroform and the extract washed with an aqueous solution of sodium bicarbonate and finally with water. The dark sirup obtained on solvent removal of the dried (decolorizing charcoal) extract was dissolved in benzene and petroleum ether added to incipient opalescence. After standing overnight at icebox temperature the supernatant liquid was removed by decantation and the separated sirup was crystallized from 50% ethanol; yield 0.32 g., m. p. 95°. Pure material was obtained on recrystallization from ethanol and from methanol; yield 0.10 g., m. p. 100–102° (mixed m. p. unchanged), spec. rot. +10° (20°; *c*, 2, abs. EtOH). Micheel and co-workers[9] report for *aldehydo-d*-galactose heptaacetate m. p. 103°, spec. rot. +10° (EtOH).

**Di-(1-chloro-*aldehydo-d*-galactose Pentaacetate) Methyl Phosphate (III).**—This substance was prepared according

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(6) All specific rotations are recorded to the D-line of sodium light; 26° is the temperature; *c* is the concentration in grams per 100 cc. of solution.

(7) A. Kunz and C. S. Hudson, THIS JOURNAL, **48**, 1982 (1926).

(8) M. L. Wolfrom, *ibid.*, **53**, 2275 (1931).

(9) F. Micheel, H. Ruhkopf and F. Suckfüll, *Ber.*, **68**, 1523 (1935).

to the procedure described for the corresponding ethyl compound (II) except that 150 parts of methanol was used in place of the ethanol. A good yield was obtained; m. p. 187–188° (dec.), spec. rot. −19° (30°; *c*, 4.2; $CHCl_3$). The substance crystallized in rod-shaped prisms and showed solubilities and behavior similar to II.

*Anal.* Calcd. for $C_{32}H_{44}O_{23}(OCH_3)Cl_2P$: $OCH_3$, 3.35. Found: $OCH_3$, 3.97.

**1,1-Dichloro-*aldehydo-d*-galactose Pentaacetate (IV).**—*aldehydo-d*-Galactose pentaacetate (10 g., 1 mol) was dissolved in 100 cc. of pure benzene, 15 g. of Drierite (anhydrous calcium sulfate) added and the whole refluxed in an all-glass apparatus equipped with a drying tube. Powdered phosphorus pentachloride (6.8 g., 1.3 mol) was introduced quickly and the reflux maintained for twelve hours, whereupon the pale yellow solution was filtered and the filtrate washed with ice water and with an aqueous solution of sodium bicarbonate until halogen free (eight to twelve washings). Solvent removal from the dried (decolorizing charcoal) solution left 3 to 5 g. of a pale yellow sirup. This sirup was dissolved in the minimum quantity of hot ethanol and was crystallized on the addition of an equal volume of water. Pure material was obtained on further recrystallization from 80% ethanol; yield 0.8–1.6 g. of m. p. 148–150°; spec. rot. +11° (20°; *c*, 3.2; $CHCl_3$). The substance was soluble in the common solvents except petroleum ether and cold water. It showed no reduction toward copper acetate (see Table I) and reduced Fehling solution only on long boiling. It gave a positive Schiff test very slowly on standing.

It was found that a reflux period less than specified above (twelve hours) yielded compound I while a longer period yielded only sirups which could not be crystallized and which readily decomposed.

*Anal.* Calcd. for $C_6H_7O_5(CH_3CO)_5Cl_2$: C, 43.2; H, 4.98; Cl, 15.9. Found: C, 43.3; H, 5.07; Cl, 15.6.

We are indebted to Mr. John Walker (W. P. A. Project 18062) for assistance rendered in the analytical determinations. We also acknowledge the general assistance of Mr. Irving Auerbach (N. Y. A. Project O. S. U. 167).

## Summary

1. The action of phosphorus pentachloride upon *aldehydo-d*-galactose pentaacetate in dry benzene produces a crystalline substance (IV) which is shown to be 1,1-dichloro-*aldehydo-d*-galactose pentaacetate.

2. The action of phosphorus pentachloride upon *aldehydo-d*-galactose pentaacetate in ether leads to the isolation of a crystalline substance (I) designated di-(1-chloro-*aldehydo-d*-galactose pentaacetate) chlorophosphate.

3. From I is obtained di-(1-chloro-*aldehydo-d*-galactose pentaacetate) ethyl (and methyl) phosphate, II, and III.

4. The structure assigned to I is made probable by its hydrolysis to *aldehydo-d*-galactose pentaacetate and by its reaction with ethanol to form II, from which *aldehydo-d*-galactose heptaacetate is obtained on acetylation.

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# Crystalline Phenylurethans (Carbanilates) of Sugar Glycosides

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A well-established procedure in organic chemistry is the characterization of carbinols as N-aryl urethans prepared by the reaction of N-aryl isocyanates with the carbinol. Maquenne and Goodwin[1] investigated the extension of this reaction, using phenyl isocyanate, to a number of unsubstituted sugars but obtained only amorphous powders. Jolles and Botrini,[2] likewise employing phenyl isocyanate, obtained as amorphous powders the phenylurethans or carbanilates of several naturally occurring glycosides. Crystalline fully substituted carbanilates of some of the sugar alcohols have been reported.[1,3]

We have now been successful in obtaining in crystalline form the carbanilates of four of the methyl glycosides of the sugars, in which derivatives all of the free hydroxyls have been brought into reaction. These substances melt with decomposition at high temperatures and exhibit correspondingly low solubilities. Under certain conditions they show a pronounced tendency to separate as gels and are in general rather difficult to manipulate.

These polyurethans or polycarbanilates were not sufficiently soluble in chloroform for satisfactory polarizations. Rotations are recorded in acetone solution for all except β-methyl-*d*-glucoside tetracarbanilate, for which pyridine was found to be the only suitable polarization sol-

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[1] L. Maquenne and W. Goodwin, *Bull. soc. chim.*, [3] **31**, 430 (1904).

[2] E. Jolles and M. Botrini, *Gazz. chim. ital.*, **65**, 1217 (1935).

[3] H. Tessmer, *Ber.*, **18**, 968 (1885).