NOTE.

258. *The Action of Phosphorus Pentachloride on* 1 : 2-5 : 6-*Di*-O-iso-*propylidene*-D-*glucofuranose.*

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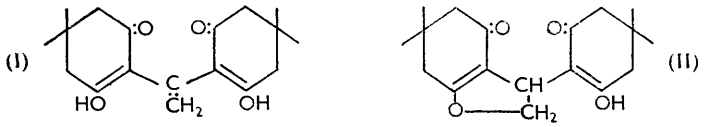
PHOSPHORUS PENTACHLORIDE converts 1 : 2-5 : 6-di-*O-iso*propylidene-D-glucofuranose into a monochloromonodeoxy-di-*O-iso*propylidene hexose which was assigned the structure of 3-chloro-3-deoxy-1 : 2-5 : 6-di-*O-iso*propylidene-D-glucofuranose.[1] However this product is dextrorotatory, whereas derivatives of 1 : 2-5 : 6-di-*O-iso*propylidene-D-glucofuranose are all lævorotatory,[2,3] and hydrolysis yielded a monochloromonodeoxyhexose whose constants {m. p. 135—136°, $[\alpha]_D^{20}$ +92·5° ⟶ +46·6° (equil.)}, while not agreeing with those published for 3-chloro-3-deoxy-D-glucose [3] (m. p. 155—156°, $[\alpha]_D^{20}$ +64·1°), are reasonably close to those published for 6-chloro-6-deoxy-D-glucose [4] {m. p. 135—136°, $[\alpha]_D^{19}$ +78° ⟶ +35° (equil.)}. The product of hydrolysis has now been characterised as 6-chloro-6-deoxy-D-glucose by periodate oxidation, and by conversion into 3 : 6-anhydro-β-D-glucofuranose.

The monochloromonodeoxyhexose consumed 3·96 mols. of periodate, releasing 3·60 mols. of titratable acid. On reduction of excess of periodate with ethylene glycol, addition of standard alkali and back-titration, 5·00 mols. of alkali were found to be consumed by the oxidation products. If, instead of removing excess of periodate, the oxidation products were rendered first alkaline, then acid, 4·91 mols. of periodate were found to be consumed, 5·52 mols. of titrable acid were produced, and 0·72 mol. of formaldehyde was isolated as the the dimedone derivative. All these figures are consistent with the production of chloroacetaldehyde in the primary reaction with periodate, which was then hydrolysed by alkali to glycollaldehyde and oxidised by periodate to formaldehyde.

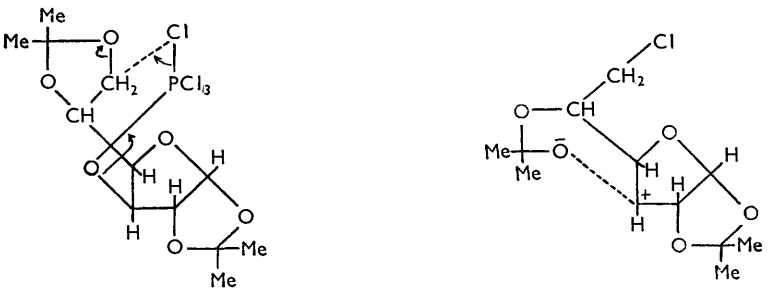
[1] Allison and Hixon, *J. Amer. Chem. Soc.*, 1926, **48**, 406.
[2] Vogel and Georg, " Tabellen der Zucker und ihrer Derivate," Springer, Berlin, 1931, p. 362.
[3] Newth, Overend, and Wiggins, *J.*, 1947, 10.
[4] Helferich and Bredereck, *Ber.*, 1927, **60**, 1995.

Treatment of the initial products of periodate oxidation with dimedone gave a derivative (I), $C_{18}H_{24}O_4$, m. p. 183—187°. Refluxing with hydrochloric acid in ethanol converted this into an isomeric compound (II), m. p. 231—233°. Chloroacetal and dimedone also yielded the first isomer (I). Glycollaldehyde and dimedone yielded the second isomer (II). Titration with alkali showed that isomer (I) possesses two β-keto-enol groups, whereas isomer (II) possesses one β-keto-enol group. Comparison of their ultraviolet absorption spectra in weakly acid and in alkaline solution confirmed this conclusion. Isomers (I) and (II) must therefore have the annexed structures.



This identifies chloroacetaldehyde as a product of periodate oxidation of the sugar, and so the latter must have the structure of a 6-chloro-6-deoxyhexose. Confirmation of the *gluco*-configuration was obtained by converting the 6-chloro-6-deoxyhexose into a mixture of anomeric glycosides. This was oxidised by periodate, consuming 2·0 mols. of oxidant and releasing 1·0 mol. of titratable acid, so indicating a pyranoside structure. The glycoside was hydrolysed to a crystalline but extremely hygroscopic methyl anhydrohexopyranoside. Hydrolysis of this afforded 3 : 6-anhydro-β-D-glucofuranose, m. p. 122—123°, $[\alpha]_D^{20}$ +53·8° (cf. ref. 5). Since this sequence of reactions does not involve a change of configuration at any of the asymmetric centres,[6] the 6-chloro-6-deoxyhexose must be 6-chloro-6-deoxy-D-glucose.

Migration of the *iso*propylidene group from the 5 : 6- to the 3 : 5-position can be pictured as resulting from an S_Ni' mechanism of chlorination.



Experimental.—Chlorination of 1 : 2-5 : 6-*di*-O-iso*propylidene*-D-*glucofuranose.* Phosphorus pentachloride (50 g.), sodium carbonate (freshly ignited; 40 g.), and light petroleum (0·5 l.; b. p. 80—100°; purified over concentrated sulphuric acid, washed, distilled, and dried) were stirred for 1 hr., protected from moisture. Then 1 : 2-5 : 6-di-*O-iso*propylidene-D-glucofuranose (40 g.) and sodium carbonate (freshly ignited; 40 g.) were added, and the whole was stirred vigorously at room temperature for 2 hr. and at 60° for 2 hr. The light petroleum was decanted, shaken with 15% aqueous sodium hydroxide (1 l.) for 12 hr., washed, and evaporated to a syrup (9·5 g.). This was passed in benzene through alumina (Peter Spence, "H") and evaporated, giving 6-*chloro*-6-*deoxy*-1 : 2-3 : 5-*di*-O-iso*propylidene*-D-*glucofuranose* (4·0 g.), b. p. (short-path) 120°/0·05 mm., n_D^{20} 1·4734, $[\alpha]_D^{20}$ +35·4° (*c* 1·95 in MeOH) (Found: C, 52·0; H, 6·7; Cl, 13·0. $C_{12}H_{19}O_5Cl$ requires C, 51·8; H, 6·9; Cl, 12·7%).

6-*Chloro*-6-*deoxy*-D-*glucose.* 6-Chloro-6-deoxy-1 : 2-3 : 5-di-*O-iso*propylidene-D-glucofuranose (4·58 g.) in methanol (100 c.c.) and N-sulphuric acid (30 c.c.) was refluxed for 9 hr. The solution was freed from acid with Amberlite resin IR-4B, and evaporated to a glass (3·19 g.). When moistened with acetone and kept, this eventually crystallised. Recrystallised from ethanol–ether at 5°, it gave 6-chloro-6-deoxyglucose as needles, m. p. 135—136°, $[\alpha]_D^{20}$ +92·5° ⟶ +46·6°

[5] Fischer and Zach, *Ber.*, 1912, **45**, 456.
[6] Peat, *Ann. Reports*, 1939, **36**, 261.

(equil.) (*c* 7·6 in H_2O) (Found : C, 36·5; H, 5·8. Calc. for $C_6H_{11}O_5Cl$: C, 36·3; H, 5·6%), whose *phenylosazone* had m. p. 167—171° (Found : C, 57·4; H, 5·6; N, 14·4; Cl, 9·9. $C_{18}H_{21}O_3N_4Cl$ requires C, 57·4; H, 5·6; N, 14·9; Cl, 9·4%).

Periodate oxidation of 6-*chloro*-6-*deoxy*-D-*glucose*. A solution of 6-chloro-6-deoxy-D-glucose (136 mg.) in 0·090M-sodium metaperiodate (50 c.c.) was kept at room temperature. Excess of periodate was determined by Barneby's method.[7] Free acid was determined after reducing excess of periodate with ethylene glycol, either by titrating aliquots with 0·01N-sodium hydroxide to the end-point of screened methyl-red (forward titration), or by treating aliquot parts (1 c.c.) with 0·01N-sodium hydroxide (10 c.c.) and then titrating them with 0·01N-sulphuric acid to the end-point of screened methyl-red (backward titration).

Time (min.)	5	25	65	115	330
Periodate consumed (mols.)	2·66	3·35	3·77	3·94	3·96
Time (min.)	15	37	65	115	480
Acid released (forward titrn.) (equiv.)	2·04	2·65	3·01	3·30	3·60
Time (min.)	10	40	65	115	330
Acid released (backward titrn.) (equiv.)	3·48	4·31	4·70	4·94	5·00

Aliquot parts (1 c.c.) of the solution were treated with 0·1N-sodium hydroxide (1 c.c.), kept 1 hr., then treated with 0·1N-sulphuric acid (1 c.c.); periodate consumed (estimated as above) was 4·91 mols.; acid released (forward titration) was 5·52 mols.; formaldehyde recovery (method of Reeves [8]) was 0·72 mol.

Preparation of keten–dimedone complex (I). (*a*) From 6-chloro-6-deoxy-D-glucose. A solution of 6-chloro-6-deoxy-D-glucose (104 mg.) in water (5 c.c.) and 0·30M-sodium metaperiodate (10 c.c.) was kept for 4 hr. at room temperature, then treated with N-hydrochloric acid (10 c.c.), then 1·2N-disodium hydrogen arsenite (10 c.c.), followed after disappearance of the iodine, by M-sodium acetate (20 c.c.) and dimedone (400 mg.) in 95% ethanol (5 c.c.). After 12 hr. the precipitate was filtered off, washed with water, and dried (52 mg.). The *compound* (I) formed needles (from ethanol–water), m. p. 183—187° (Found : C, 71·1; H, 8·3. $C_{18}H_{24}O_4$ requires C, 71·0; H, 7·9%).

(*b*) From chloroacetal. A solution of dimedone (300 mg.) in 95% ethanol (4 c.c.), acetic acid (1 c.c.), M-sodium acetate (5 c.c.), and water (20 c.c.) was heated with chloroacetal (0·15 g.). Crystals (200 mg.) separated, this compound forming needles (from ethanol–water), m. p. and mixed m. p. 183—187° (Found : C, 70·5; H, 8·1%).

Preparation of dimedone complex (II). (*a*) From glycollaldehyde. Dihydroxymaleic acid (1·5 g.) in water (5 c.c.) was heated at 80° until decarboxylation was complete. A yellow solid was filtered off and discarded. The filtrate and washings (10 c.c.) were treated with dimedone (2·5 g.) and piperidine (1 c.c.) in methanol (40 c.c.). After refluxing for 10 min., the methanol was distilled off *in vacuo*. The product separated as an oil which eventually crystallised (1·35 g.). Recrystallised from ethanol–water, *compound* (II) had m. p. 231—233° (Found : C, 70·9; H, 8·1%).

(*b*) From keten–dimedone complex (I). The compound (I) (100 mg.), 95% ethanol (3 c.c.), and concentrated hydrochloric acid (3 drops) were refluxed for 10 min., diluted with water, and extracted with ether. The extract was washed and evaporated to a glass (100 mg.). Recrystallised from ethanol–water, compound (II) had m. p. and mixed m. p. 231—233°.

Estimation of β-*keto-enol groups*. (*a*) By potentiometric titration. The amount of alkali neutralised by each dimedone derivative at pH 10 was : compound (I) 2·00 equivs., (II) 1·01 equivs.

(*b*) By ultraviolet light absorption. See Table.

	Acidified EtOH		0·2N-Sodium hydroxide	
Solvent :	$\lambda_{max.}$	log ε	$\lambda_{max.}$	log ε
Acetaldehyde–dimedone compound	259	4·36	285	4·69
Compound (I)	261	4·37	285	4·63
Compound (II)	267	4·42	287	4·52

Methyl 6-*chloro*-6-*deoxy*-αβ-D-*glucopyranoside*. 6-Chloro-6-deoxy-D-glucose (1·36 g.) and 2% hydrogen chloride in methanol were refluxed for 8 hr., neutralised with silver carbonate,

[7] Barneby, *J. Amer. Chem. Soc.*, 1916, **38**, 330.
[8] Reeves, *ibid.*, 1941, **63**, 1476.

filtered, and evaporated to a syrup (1·19 g.) (Found : C, 39·7; H, 6·1. Calc. for $C_7H_{13}O_5Cl$: C, 39·6; H, 6·2%). A solution of this glycoside (97·9 mg.) in 0·0636M-sodium metaperiodate (25 c.c.) was kept at room temperature.

Time (min.)	4	20	55	137	270	1202
Periodate consumed (mols.)	0·12	0·61	1·23	1·61	1·84	2·05
Time (min.)	4	21	58	139	277	1202
Acid released (equiv.)	0·08	0·25	0·50	0·72	0·84	1·00

Methyl 3 : 6-*anhydro*-αβ-D-*glucopyranoside.* Methyl 6-chloro-6-deoxy-αβ-D-glucopyranoside (0·97 g.), ethanol (20 c.c.), and N-sodium hydroxide (10 c.c.) were refluxed for 3 hr., neutralised with carbon dioxide, evaporated, and extracted with boiling acetone. The extract, on evaporation, gave a syrup (0·46 g.), b. p. (short-path) 90°/0·05 mm. The distillate crystallised but was very deliquescent (Found : C, 47·7; H, 6·9. Calc. for $C_7H_{12}O_5$: C, 47·7; H, 6·9%).

3 : 6-*Anhydro*-β-D-*glucofuranose.* Methyl 3 : 6-anhydro-αβ-D-glucopyranoside (0·36 g.) and 0·1N-sulphuric acid (5 c.c.) were heated at 100° for 3 hr. The solution was freed from acid with Amberlite resin IR-4B, and evaporated, leaving a crystalline residue (0·27 g.) which formed needles, m. p. 122—123°, $[\alpha]_D^{20}$ +53·8° (*c* 1·9 in H_2O), from ethanol–ethyl acetate–light petroleum (Found : C, 44·5; H, 6·2. Calc. for $C_6H_{10}O_5$: C, 44·4; H, 6·2%).

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