

guanidine sulfate, *p*-tolylguanidine hydrochloride, α -methyl α -phenylguanidine hydrochloride and β -phenylethylguanidine sulfate.

2. A corrected formula and melting point for *p*-tolylbiguanide hydrochloride have been reported.

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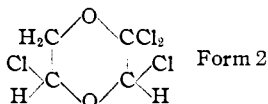
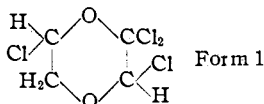
Derivatives of Dioxane

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In a previous communication¹ we mentioned the first results of a research on the chlorination of 1,4-dioxane. 2,3-Dichlorodioxane, the first product of chlorination, was separated; the chlorine atoms proved to be very mobile as they are in all α -chloro ethers. With sodium ethylate we isolated the 2,3-diethoxydioxane, while with glycol the two isomeric naphthodioxanes (1,4,1',4'-tetroxadecahydronaphthalene). These investigations were continued in different directions.

A. The Action of Chlorine on Dioxane.—Neither repeated distillation nor investigation of the products of hydrolysis of the first fraction gave any indication of the existence of monochlorodioxane. The investigation of the mechanism of the first stage of the chlorination is still being continued.

On chlorinating dichlorodioxane, it appeared that chlorine is rapidly absorbed. The first time the chlorination was continued for sixteen hours at 130–150° and the product was carefully fractionated. The first fraction, boiling below 102° (15 mm.), appeared to have a chlorine content corresponding with tetrachlorodioxane. Hydrolysis by means of boiling water produced glycolic aldehyde. Subsequent treatment with dinitrophenylhydrazine gave the dinitrophenylhydrazone of glycolic acid and the dinitrophenylosazone of glycolic aldehyde. The quantity of these precipitates was in accordance with the expectation, based on the decomposition of one of the following tetrachlorodioxanes



Butler and Cretcher² succeeded, after a chlorination of twelve hours, in the isolation of a crystalline asymmetrical and two isomeric symmetrical tetrachlorodioxanes besides the liquid asymmetrical one, just mentioned. In the higher-boiling fractions of the product obtained by the chlorination of dichlorodioxane during sixteen hours, only very little oxalic acid could

(1) *Rev. trav. chim.*, **50**, 909 (1931); *Proc. Acad. Sci.*, **34**, 631 (1931).

(2) Butler and Cretcher, *THIS JOURNAL*, **54**, 2987 (1932).

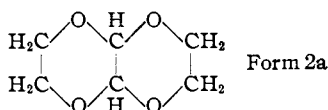
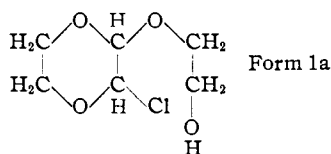
be detected after decompn. with water, so that we may conclude that tetrachlorodioxane, with all the four chlorine atoms at one side of the molecule, is hardly formed. The odor of the chlorinated dichlorodioxane reminds us of acid chlorides, but ammonia did not yield an amide and cold silver nitrate solution did not yield more than a very little precipitate, so that with this chlorination very little or no acid chloride is formed.

The second time the chlorination was continued for twenty-four hours. The reaction product was repeatedly fractionated in the apparatus of Widmer;³ the liquid was divided in seven fractions, but none of these fractions had a constant boiling point. The first fraction had a chlorine content almost agreeing with pentachlorodioxane and the last fraction a chlorine content little less than hexachlorodioxane.

The third time we chlorinated for about fifty hours at 110° and also at 50°. After fractionation it was possible to obtain crystals in some fractions by cooling. The second fraction of the latter chlorination yielded beautiful big crystals of a hexachlorodioxane, the last fractions of the other chlorination mixed crystals of two compounds, containing more chlorine than the hexachlorodioxane.

The hexachlorodioxane, melting at 89.5–91.0° and having the odor of camphor, is not destroyed by boiling with silver nitrate or potassium hydroxide solution in alcohol. The liquid part of the fractions appeared to be hygroscopic in a high degree. With gaseous ammonia they yielded immediately in dry ether solution a bulky white precipitate, which is also the case with cold silver nitrate solution, so that probably the ring structure is broken with the formation of acid chloride.

B. Reactions of Dichlorodioxane.—As we previously mentioned dichlorodioxane forms by boiling with glycol two isomeric naphthodioxanes. We have also to mention a publication of Donciu.⁴ Donciu isolated out of the product, obtained by the action of chlorine on glycol, crystals to which he credited the formula 1a. Treatment of this compound with sodium gave a product, m. p. 134–135°, to which he assigned formula 2a, and which he also could obtain by the action of glycol on glyoxal.



As the compound to which Donciu credited formula 2a is identical with the higher melting isomeride of naphthodioxane, the formulas suggested by him appear to be the right ones. The melting points of the two isomerides, in as pure a condition as we could get, are 111–112° and 135–136°. After

(3) Widmer, *Dissertation*, Zürich, 1925.

(4) Donciu, *Sitzber. Kais. Acad. Wiss.*, [C] 4, 2b, 7 (1895).

careful sublimation of the mixture of the two isomers in the apparatus of Kempf, the melting point of the sublimate was observed with a microscope on a electrically heated object table.⁵ All crystals appeared to melt near the melting point of the eutectic mixture of the mixture (87°), so that it is highly probable that the difficulty of the separation is due to the formation of mixed crystals; also Donciu met with great difficulties in the purification of the higher melting isomeride. Within a short time we hope to describe the properties of the isomerides more fully and also of the reaction product of trimethyleneglycol, which consists of at least two isomers.

Dichlorodioxane reacts with pyrocatechol in boiling xylene; crystals of m. p. 74–76° were obtained (see formula 3).⁶

The action of benzyl alcohol results in the greasy-looking white crystals of formula 4, m. p. 66–68°.

It seemed interesting to investigate the action of the esters of the tartaric acids on dichlorodioxane. Theoretically ten isomers are possible. With the ethyl ester of *d*-tartaric acid we obtained only one of the three possible compounds, m. p. 93.3–94.7°, for which $[\alpha_D^{22}]$ in a 0.8% alcoholic solution was determined to be -0.30° . The composition agreed with formula 5.

The ester of the *anti*-tartaric acid also reacts with dichlorodioxane, but we did not succeed in separating from the reaction product a pure compound.

Dichlorodioxane does not react with boiling acetic acid; the reaction proceeds, however, if a few drops of strong sulfuric acid are added. By pouring out the reaction mixture in water an amorphous precipitation occurs of a white compound insoluble in all normally applied organic solvents. This compound is not the diacetate of dioxane, which can conveniently be prepared by the action of potassium acetate in a solution of acetic acid on dichlorodioxane. The diacetate of dioxane (see formula 6), white crystals of m. p. 104–105.5°, shows a remarkable stability toward dilute potassium hydroxide or acid solution.

The reaction of dichlorodioxane with sodium iodide is noteworthy, because of the liberation of iodine. In boiling acetone iodine is liberated and precipitation of sodium chloride occurs. It might seem that dioxene is formed. When we try to prepare the dioxene by removing the chlorine atoms by light metals in solutions of high-boiling solvents, the metal is coated with a black tar, which can be due to polymerization of the dioxene and which prevents further reaction.

Experimental Part

Reaction with (1) Pyrocatechol.—Eleven grams of catechol and 15.6 g. of dichlorodioxane were boiled for about a week in 40 cc. of dry xylene. After distillation of the xylene *in vacuo* a brown, sticky substance remained which gave a crystalline mass by distillation in high vacuum. Three recrystallizations in ether furnished crystals of

(5) Derox, Dissertation, Delft, 1922.

(6) Cf. R. Summerbell and R. Christ, *THIS JOURNAL*, **54**, 3777 (1932).

m. p. 74–76°. The pale yellow color is probably due to impurity. The amount of the compound was 5 g.

Anal. Calcd.: mol. wt., 194; C, 62.1; H, 5.1. Found: mol. wt., 190; C, 62.3, 62.2; H, 5.3, 5.1.

(2) **Benzyl Alcohol.**—7.5 g. of benzyl alcohol was heated with 5.0 g. of dichlorodioxane until no more hydrogen chloride was liberated. The brown reaction product was distilled in high vacuum. The oil thus obtained crystallized for the larger part in about four days. Recrystallizations in ligroin and alcohol gave 2 g. of flat, greasy-looking crystals, m. p. 66–68°, very soluble in all common organic solvents and insoluble in water.

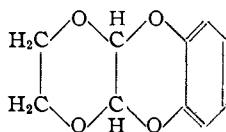
Anal. Calcd.: C, 72.0; H, 6.7. Found: C, 72.1, 72.3; H, 6.4, 6.5.

(3) **Diethyl Ester of *d*-Tartaric Acid.**—6.7 g. of di-ethyl ester of *d*-tartaric acid and 5.0 g. of dichlorodioxane were heated until the production of hydrogen chloride stopped. The brown reaction product was distilled in high vacuum. The fraction distilling between 130 and 150° crystallized. Three recrystallizations from alcohol gave needle-like crystals of m. p. 93.3–94.7°, which are but sparingly soluble in ether and alcohol (less than 2%) at 20°; $[\alpha_D^{22}] -0.30$ for a 0.8% alcoholic solution. The amount of the pure substance was 2.0 g.

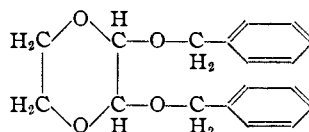
Anal. Calcd.: C, 49.5; H, 6.2. Found: C, 48.8; H, 6.1.

(4) **Potassium Acetate.**—19.1 g. of anhydrous potassium acetate and 15.1 g. of dichlorodioxane were dissolved in 70 cc. of dry acetic acid. The reaction was initiated by heating and proceeded vigorously with evolution of heat. The precipitated potassium chloride was filtered and the acetic acid was distilled off *in vacuo*. The brown oily substance thus obtained was distilled in high vacuum. After recrystallization from ether we obtained 4.8 g. of fine, white needle-shaped crystals, m. p. 104–105.5°.

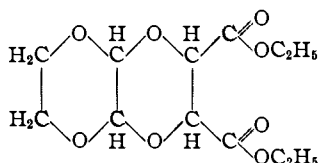
Anal. Calcd.: C, 47.1; H, 5.7. Found: C, 47.1; H, 5.9.



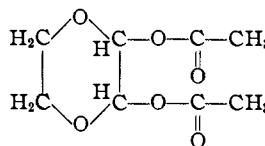
Form 3



Form 4



Form 5



Form 6

Tetrachlorodioxane.—Thirty grams of dichlorodioxane was chlorinated during sixteen hours at 130–150°. The fraction boiling below 102° (15 mm.) led to the following analyses: chlorine found, 63.1, and 63.1%; calcd., 63.1%. 6.4 mg. of the liquid was heated with 20 cc. of water in a closed tube in boiling water. Destruction with boiling water in an Erlenmeyer flask with reflux condenser is not possible, for the small quantity of the liquid creeps into the condenser, so that it is not attacked by the water. After the hydrolysis the quantity of the precipitate with dinitrophenylhydrazine was determined; this proved to be 18.0 mg., while the theoretically calculated amount for formulas 1 or 2 is 19.0 mg. A test with pure dichlorodioxane under the same conditions showed that the amount of hydrazone experimentally found does not exceed 95% of the calculated

value. These analyses, in addition to the fact that glycolic aldehyde can be indicated after the hydrolysis with water and that dinitrophenylhydrazine produces two different precipitations enable us to conclude that the choice must be between the formulas 1 and 2.

After chlorinating 50 g. of dichlorodioxane during twenty-four hours (140°), we obtained a mixture with a chlorine content of about 5.5% for 1 dioxane, out of which we could not separate any constant boiling fraction nor any crystals, notwithstanding the fact that we submitted the liquid to very careful repeated fractionation.

Hexachlorodioxane.—Forty grams of dichlorodioxane was chlorinated for about fifty hours at 60°. From the second fraction hexachlorodioxane separated after cooling in ice (2 g., m. p. 89.5–91°).

Anal. Calcd.: C, 16.3; H, 0.7; Cl, 72.2; O, 10.8; mol. wt., 295. Found: C, 16.2; H, 0.9; Cl, 72.2; O, 10.8; mol. wt., 300.

The oxygen was determined by the direct method of ter Meulen, the mol. wt. by the method of Rast; all values are the average of at least two analyses. Forty grams of dichlorodioxane was chlorinated for about fifty hours at 110°. After distillation we obtained a crystalline residue, which was purified from brown impurities by distillation in high vacuum. The melting point of the mixture thus obtained was 54–60°.

Carefully fractionated precipitation by means of water, out of the alcoholic solution, was not adequate for the isolation of one of the components in pure condition; the compounds of which the mixture consists form mixed crystals. The chlorine content of the mixture is about 76%.

Once more we lay stress on the extreme stability of the hexachlorodioxane and the above-mentioned mixture of highly chlorinated products. The chlorine is not removed by boiling alcoholic potassium hydroxide or silver nitrate solution. The chemical investigation of the structure of these compounds will therefore prove to be very difficult if not impossible.

Summary

By chlorinating dichlorodioxane we isolated one liquid asymmetrical tetrachlorodioxane and a hexachlorodioxane. Higher chlorinated products are under study. It is highly probable that by long duration of the chlorination the ring structure is broken through. There are no indications of the existence of mono-, tri- and pentachlorodioxane. The stability of the chlorinated dioxanes increases greatly with increasing chlorine content, the stability of the hexachlorodioxane being so great as to prevent the investigation of its structure. The reaction products of dichlorodioxane with pyrocatechol, benzyl alcohol, diethyl ester of *d*-tartaric acid, and potassium acetate are isolated; no isomerides are found by these compounds, which is remarkable in face of the fact that glycol and trimethyleneglycol both give isomerides.

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