0.52 and indicates that some Cu^{++} reduction is perhaps caused by material other than the —SH of the R SH.

The possibility of the occurrence of this series of reactions or any of its steps must be considered when isolating (as from biological material) R SH compounds (in the presence of oxidizing agents) or R S S R by means of cupric or cuprous salts, since sulfonic acids may result which cannot be easily reconverted into the original acids. Such reactions may also take part in the oxidation of R SH and R S S R when copper salts are used as catalysts.

The reaction is of chemical interest as an example of the interaction of two substances in higher states of oxidation to produce more reactive reducing substances and some of a more fully oxidized, unreactive product. The mechanism will be more fully discussed in a subsequent publication on the production of R SO_3H from R S S R by oxidizing agents.

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THE PREPARATION OF DI- AND ISOMERIC TETRACHLORODIOXANES

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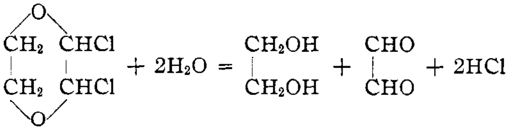
Dichlorodioxane was recently prepared by Böeseken, Tellegen and Henriques[1] for use as an intermediate in the preparation of stereoisomeric 1,4,5,8-naphthodioxanes. A convenient means of determining the structure of the dichloro derivative was found in the easy hydrolysis of the substance in boiling water. As the aqueous solution of the hydrolysis product yielded quantitatively one molecular equivalent of glyoxal-*p*-nitrophenylosazone on treatment with *p*-nitrophenylhydrazine, it was concluded that the chlorine atoms were in vicinal positions. The hydrolysis apparently proceeded according to equation I. In the present paper, this work was confirmed and the evidence in support of equation I was completed by the identification of glycol, as dibenzoate, among the hydrolysis products. As far as the present authors are aware, no other experiments on the chlorination of dioxane have been made. Van Alphen[2]



(I)

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[1] Böeseken, Tellegen and Henriques, *Proc. Roy. Soc. Amsterdam*, **34**, 631 (1931); *Rec. trav. chim.*, **50**, 909 (1931).

[2] Van Alphen, *ibid.*, **49**, 1040 (1930).

attempted to brominate the substance by warming the bromine addition compound, $C_4H_8O_2Br_2$, but could isolate only ethylene bromide and aqueous hydrobromic acid from the reaction product.

Dioxane is now a commercial product, but its chemistry has been incompletely studied. It was thought by the present authors, therefore, that further investigation of its chlorinated derivatives would be of interest. The present paper consists of a report on the preparation and chemistry of dichloro- and of several isomeric tetrachlorodioxanes.

It is well known that glyoxal is a highly reactive substance and a useful reagent in many syntheses. As the usual method of preparation[3] is inconvenient, it appeared to be worth while to investigate the use in glyoxal condensations of solutions prepared by hydrolyzing dichlorodioxane. Employing this source of glyoxal, the *p*-nitrophenylosazone was prepared in quantitative yield by reaction with *p*-nitrophenylhydrazine; the diurea condensation product glycoluril,[4] was isolated in 70% yield; and from the latter hydantoin was prepared in 67% yield. Thus it is apparent that dichlorodioxane is a practical source of glyoxal for reactions of this type.

Dichlorodioxane.—This substance was prepared according to Böeseken, Tellegen and Henriques;[1] 208 g. of dioxane yielded 233 g. of pure dichlorodioxane boiling at 88–89° at 16–17 mm.; yield, allowing for 15 g. of recovered dioxane, 67.7%.

Glycol Dibenzoate.—1.6 g. of dichlorodioxane was decomposed by warming in 25 cc. of boiling water. A clear solution was obtained after about ten minutes' heating. The reaction mixture was cooled, made alkaline with sodium hydroxide and treated with benzoyl chloride in the usual way. The alkali-insoluble ester was extracted with ether and recrystallized from methyl alcohol. It melted at 70–72° on rapid heating.

Glyoxal-*p*-nitrophenylosazone.—1.6 g. of dichlorodioxane was decomposed as described above. An abundant red precipitate, which was formed on addition of an aqueous solution of 4 g. of *p*-nitropenylhydrazine hydrochloride to the cooled hydrolysis product, was filtered and washed with water and alcohol; yield, 3.2 g. of pure product melting at 306°, or 97% of the theoretical.

Glycoluril.—1.6 g. (1 mol) of dichlorodioxane was decomposed in 25 cc. of boiling water and the resulting acidic solution of glyoxal was mixed with an aqueous solution of 1.3 g. (2 mols) of urea. The mixture was warmed to the boiling point and then set aside. White crystals of glycoluril soon began to separate from the solution. After standing for several hours these were filtered, washed and dried. The yield was 1.0 g., or 70% of the theoretical; 15.6 g. of dichlorodioxane when treated similarly gave 8.7 g. of glycoluril, or 61.3% of the theoretical. The substance did not melt below 330°.

Hydantoin.—Nine grams of glycoluril was mixed with 36 g. of 25% hydrochloric acid and the mixture evaporated on a hot water bath until it weighed only 21 g.[3] Hydantoin crystallized from the solution on cooling in the ice box. A further quantity was obtained on evaporation of the mother liquor. The product was recrystallized from water. The yield of purified hydantoin melting at 214° was 4.3 g., or 67% of the theoretical.

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[3] Siemonsen, *Ann.*, **333,** 111 (1904).

[4] Schiff, *ibid.*, **189,** 157 (1877); Bottinger, *Ber.*, **10,** 1923 (1877); Widman, *ibid.*, **19,** 2477 (1886); Biltz, *ibid.*, **40**, 4808 (1907); see also Pauly and Sauter, *ibid.*, **63B,** 2063 (1930).

The previous authors[1] also prepared diethoxydioxane by reaction of the dichloro compound with sodium ethylate. The method was improved in the present work by the substitution of absolute alcohol for sodium ethylate as reagent.

An attempted bromination gave the same negative results as were obtained by Van Alphen.[2]

Diethoxydioxane.—15.6 g. of dichlorodioxane was warmed on a water-bath for two and one-half hours with 30 cc. of absolute alcohol. Most of the hydrogen chloride and the excess of alcohol were removed by evaporation. The residue was taken up in ether, and the ether solution was washed with sodium bicarbonate solution and with water. The ether layer was dried with anhydrous sodium sulfate. The ether was evaporated off and the residue on distillation at 14 mm. gave 12.3 g. of diethoxydioxane boiling at 95–98°, or 71% of the theoretical yield.

Attempted Bromination of Dioxane.—Ninety grams of dioxane was kept gently refluxing and during six hours 335 g. of bromine was dropped into the liquid. The mixture was warmed for seven hours longer. On distillation of the reaction product 100 g. of liquid came over under 105°. The distillate collected in two layers, which were separated in a separatory funnel. The heavy layer was washed with water and dried with calcium chloride; 65.5 g. of ethylene dibromide boiling at 128–131° was obtained. The top layer consisted of aqueous hydrobromic acid. The residual tar could not be distilled.

2,3-Dichlorodioxane is theoretically capable of existence in *cis*- and *trans*- modifications. The facts that Böeseken, Tellegen and Henriques[1] were able to prepare stereoisomeric 1,4,5,8-naphthodioxanes and that chlorination of dioxane to the dichloro stage yields a uniform product, are interesting in this connection. Thus, although this substance is a constant boiling liquid, it may contain both of the possible isomers, because, on reaction with glycol, it yields two crystalline 1,4,5,8-naphthodioxanes.

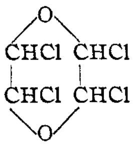
The further chlorination of dioxane was next undertaken. It was hoped that the reaction would yield symmetrical tetrachlorodioxane, as this substance would give two molecular equivalents of glyoxal if its hydrolysis proceeded in a manner similar to the decomposition shown in equation I. However, the reaction product was found to consist of a mixture of tetrachlorodioxanes.

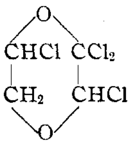
Preparation of Isomeric Tetrachlorodioxanes.—Two hundred grams of dioxane was chlorinated for twelve hours at 90°, as described previously.[1] Chlorine was then passed into the crude dichlorodioxane for twelve hours longer at 135–140°, heat being supplied by an oil-bath. Some crystalline material separated on cooling the reaction product. After standing for forty-eight hours in the ice box, the mixture was filtered, the crystals were set aside and the liquid was repeatedly fractionated at 11–12 mm.

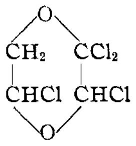
As the distillations were continued, the top fractions yielded further small amounts of crystalline material. The lowest liquid fraction, 10 g. boiling below 90°, was not further investigated. The fractions between 95 and 100° also deposited crystals as the separation progressed, leaving a liquid fraction which on redistillation had a constant boiling point of 93–95°; yield, 57 g. The crystalline material from the low-boiling fractions was recrystallized from a mixture of ether and petroleum ether of boiling range 30–40°. The yield was 35 g. of white crystals melting at 57–58°. Several small fractions (total weight 46 g.) of boiling point up to 120° were also obtained. The mixture of crystals from the crude reaction product and from the top fractions of the distilled liquid on recrystallization from ether yielded white needles melting at 143–144° in a yield of 22 g. and smaller flat crystals melting at 59–60°. The yield of the latter was 10 g.

The four main fractions on analysis gave the correct value for tetrachlorodioxane. The structures of the compounds were determined by hydrolysis in boiling water and identification of the hydrolysis products in the form of their nitrophenylhydrazine derivatives.

Because the first stage of the chlorination was carried out under conditions which yield the known 2,3-dichlorodioxane, at least two of the chlorine atoms in the tetrasubstituted derivatives are in vicinal positions. The structural possibilities for the four compounds isolated are limited by this condition to those shown.


(a)


(b)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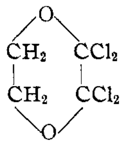
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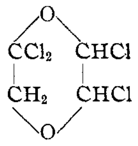
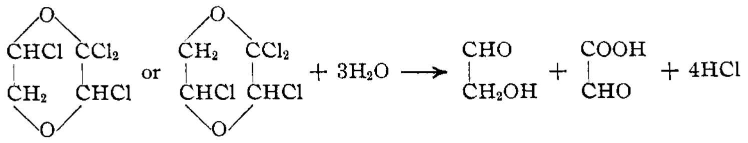

(e)

Tetrachlorodioxanes, b. p. 93–95° at 11–12 mm. and m. p. 57–58°, on decomposition with boiling water and subsequent treatment with *p*-nitrophenylhydrazine each yielded one molecular equivalent of glyoxylic acid *p*-nitrophenylhydrazone and one of glyoxal-*p*-nitrophenylosazone. The formation of glyoxylic acid on hydrolysis, together with the analytical data, indicates that these substances are tetrachlorodioxanes with three chlorine atoms on one side of the molecule and one on the other. They may be the structural isomers shown, formulas "b" and "c," or stereoisomers of either of these. The side of the molecule bearing the single chlorine atom should on hydrolysis yield glycolic aldehyde. The glyoxal-*p*-nitrophenylosazone obtained in the experiments is explained by the ease with which glycolic aldehyde is converted into this substance on treatment with *p*-nitrophenylhydrazine in acid solution.[5] The breakdown of these tetrachlorodioxanes is shown in Equation II.


Formula "b" Formula "c"

(II)

Tetrachlorodioxanes, m. p. 59–60° and m. p. 143–144°, gave two molecular equivalents of glyoxal-*p*-nitrophenylosazone when solutions obtained by decomposing them with boiling water were treated with *p*-nitrophenyl-

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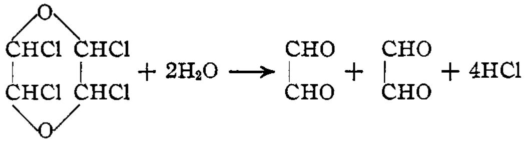
[5] Wohl and Neuberg, *Ber.*, **33**, 3107 (1900).

hydrazine. They are therefore symmetrically substituted tetrachlorodioxanes and are two of five possible geometric isomers of formula "a." Their breakdown is shown in equation III.



(III)

Formula "a"

Analyses of the Isomeric Tetrachlorodioxanes.—Calcd. for $C_4H_4O_2Cl_4$: Cl, 62.8. Found: liquid b. p. 93–95° at 11–12 mm., Cl, 62.1, d_4^{15} 1.5735; n^{25} 1.4956; crystals m. p. 57–58°, Cl, 63.1; crystals m. p. 59–60°, Cl, 63.1°, crystals m. p. 143–144°, Cl, 62.8.

Structure of the Isomeric Tetrachlorodioxanes.—Approximately 1.0-g. samples were heated under a reflux condenser with 50 cc. of water until clear solutions were obtained. The solutions were filtered and treated with 4.25 equivalents of *p*-nitrophenylhydrazine in dilute hydrochloric acid solution. A summary of the reaction products is shown in Table I.

Table I

Isomer	Sample, g.	Time of hydrolysis, hrs.	Products isolated	Calcd. yield, g.
Liquid b. p. 11–12 mm.	1.1	6	1.4 g. glyoxal *p*-nitrophenylosazone, m. p. 309°	1.6
			0.7 g. glyoxylic acid *p*-nitrophenylhydrazone[a]	1.0
Crystals, m. p. 57–58°	1.0	6	1.4 g. glyoxal-*p*-nitrophenylosazone, m. p. 306°	1.5
			0.6 g. glyoxylic acid *p*-nitrophenylhydrazone[a]	1.5
Crystals, m. p. 59–60°	1.0	2.5	2.8 g. glyoxal-*p*-nitrophenylosazone, m. p. 310°	2.9
Crystals, m. p. 143–144°	0.75	3	2.1 g. glyoxal-*p*-nitrophenylosazone, m. p. 310°	2.2

[a] This substance was identified by the facts that it darkened at about 180° and decomposed at about 200°,[6] and that it was soluble in dilute alkali to a beautiful deep red solution.

Formula "d" requires the formation of one molecule of oxalic acid and one of glycol, and formula "e" one of glycolic acid and one of glyoxal on hydrolysis. As neither of these sets of results agrees with the actual laboratory findings, these structures may be ruled out as applying to this work.

As a convenient source of glyoxal the tetrachlorodioxanes did not prove to be particularly suitable, mainly because of the low yields of symmetrically substituted compounds which give glyoxal on hydrolysis. All the compounds prepared had an odor resembling phosgene, which was more pronounced in the unsymmetrical tetrachloro derivatives. The liquid ap-

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[6] Dakin and Dudley, *J. Biol. Chem.*, **15**, 136 (1913).

peared to be less stable than the other isomers, as it developed a strong odor of hydrochloric acid and lost about 3% of its chlorine on keeping for two weeks. The chlorine atoms in all these substances are quite reactive, and hence it is possible that further study will show interesting uses to which they might be put.

Some interesting information as to the relative stability toward hydrolysis of the di- and the isomeric tetra-substituted chloro derivatives of dioxane is available as a result of these studies. While dichlorodioxane is completely broken up by warming for ten or fifteen minutes in boiling water, two and one-half to three hours of heating were required to decompose the symmetrical tetrachloro derivatives which have quite similar structures. The unsymmetrical tetrachlorodioxanes were found to be even more stable, as five to six hours heating was required for their complete decomposition.

The yields of the various products obtained from 200 g. of dioxane are shown in Table II. That they are not higher is probably due in part to the many fractional distillations required to complete the separations.

TABLE II

	Grams
Material boiling under 90° at 11–12 mm., probably largely dichlorodioxane	10
Unsym.-tetrachlorodioxane, b. p. 93–95° at 11–12 mm.	57
Unsym.-tetrachlorodioxane, m. p. 57–58°	35
Sym.-tetrachlorodioxane, m. p. 59–60°	10
Sym.-tetrachlorodioxane, m. p. 143–144°	22
Total impure higher boiling fractions	46
Total	180

Summary

Dichloro- and tetrachlorodioxanes were prepared and studied as sources of glyoxal. Four of the many possible isomeric tetrachlorodioxanes were isolated and their structures determined.

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