

binols. The Grignard reagents would be expected in most cases to yield  $\alpha$ -phenylallyl carbinols (II), while phenylallylsodium in liquid ammonia should

yield products consisting predominantly of  $\gamma$ -phenylallylcarbinols (I).

LOS ANGELES 24, CALIF.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

## The Stereochemistry of the 2,3-Dichloro-*p*-dioxanes

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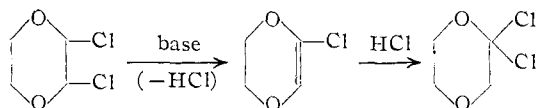
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The preparation of the second isomer of 2,3-dichloro-*p*-dioxane is described. The previously known isomer is shown to be the *trans* form by kinetic resolution with brucine, and the new isomer must therefore be assigned the *cis* configuration. Isomerization experiments show that the *trans* form is the more stable. Addition of chlorine to *p*-dioxene by means of iodobenzene dichloride results in almost exclusive formation of *trans*-2,3-dichloro-*p*-dioxane, whereas molecular chlorine gives a mixture of the *cis* and *trans* isomers, with predominance of the *cis* form. The products from various reactions of *cis*-2,3-dichloro-*p*-dioxane are the same as those from the *trans* isomer; however, there are considerable differences in the rates of the reactions. In 50% aqueous dioxane, the *cis* isomer hydrolyzes fourteen times as fast as the *trans* isomer.

### Discussion

Some years ago, Umhoefer<sup>1</sup> and later Lappin<sup>2</sup> obtained a compound, m.p. 53°, as a product in the photochlorination of dioxane in carbon tetrachloride solution. Molecular weight determination and elementary analysis indicated the formula C<sub>4</sub>H<sub>6</sub>O<sub>2</sub>Cl<sub>2</sub>, and on the basis of incomplete evidence the structure of 2,2-dichloro-*p*-dioxane was tentatively assigned. The investigation was suspended because of the apparent instability of the compound and difficulties in consistently obtaining satisfactory yields.

Recently we had need of some 2,2-dichloro-*p*-dioxane and synthesized it in satisfactory yields, using 2,3-dichloro-*p*-dioxane as starting material. The abstraction of hydrogen chloride to give chlorodioxene was achieved by means of dimethylaniline, and gaseous hydrogen chloride was then added to produce the desired 2,2-dichloro-*p*-



dioxane.<sup>3</sup> Its structure was proved by hydrolysis to *p*-dioxanone and reaction with phenylmagnesium bromide to give 2,2-diphenyldioxane.<sup>4</sup> The 2,2-dichloro-*p*-dioxane, a liquid at room temperature, had entirely different properties from the compound prepared by Umhoefer and by Lappin. Since only one isomer of this structure is possible, we decided to reinvestigate the matter.

We repeated the chlorination of dioxane in carbon tetrachloride solution and isolated the 53° compound in about 25% yield. The four possible structural arrangements for a dichlorodioxane can be differentiated by their hydrolysis products as pointed out by Boeseken, Tellegen and Henriquez.<sup>5</sup>

The 2,2-isomer would give rise to hydroxyethoxyacetic acid or its lactone. Both the 2,5- and the 2,6-isomer would yield two moles of glycolaldehyde, whereas only the 2,3-isomer would form one mole of glyoxal and glycol. When the new compound was hydrolyzed, we obtained one mole of glyoxal, determined quantitatively as *p*-nitrophenylosazone, and ethylene glycol, characterized as dibenzoate. The 2,3-structure of the new compound was also shown by its reaction with silver acetate to give a 79% yield of the known diacetate of 2,3-*p*-dioxanediol, m.p. 104°.<sup>6</sup>

The preparation of the other isomer of 2,3-dichloro-*p*-dioxane, described for the first time by Boeseken, Tellegen and Henriquez,<sup>5</sup> is generally accomplished by chlorinating dioxane at reflux temperature, which varies from 100° at the start of the reaction to about 150°, as higher boiling products accumulate. Fractionation of the reaction product after consumption of the calculated amount of chlorine yields a solid, m.p. 31°, in very good yields. The two isomers of 2,3-dichloro-*p*-dioxane have distinctively different infrared spectra, especially in the region from 8 to 12  $\mu$ . We used the peaks at 10.55  $\mu$  (53° isomer) and at 11.42  $\mu$  (31° isomer) to analyze mixtures of the two compounds. It was found that the chlorination of dioxane in carbon tetrachloride solution at reflux temperature gives rise to a mixture of 35-40% of the 53° isomer and 65-60% of the 31° isomer. The chief function of the carbon tetrachloride is to maintain a moderate reaction temperature, since the same results were obtained when dioxane was chlorinated without solvent at temperatures of about 75°. By taking samples at approximately 25, 35 and 55% completion of the reaction, we found that the ratio of the two isomers did not change during the reaction at 75°. When the reaction mixture was heated above 110°, the 53° isomer was converted gradually into the 31° isomer, the rate of conversion increasing rapidly with temperature. This explains the fact that the 53° isomer was not found in chlorinations of dioxane previously described in the literature, since most of

(1) R. R. Umhoefer, Ph.D. Dissertation, Northwestern University, 1948.

(2) G. R. Lappin, Ph.D. Dissertation, Northwestern University, 1946.

(3) Melvin J. Astle and William C. Gergel, U. S. Patent 2,756,240, have described the preparation of chlorodioxene by thermal decomposition of 2,3-dichloro-*p*-dioxane.

(4) James P. Settle, M.S. Thesis, Northwestern University, 1950.

(5) J. Boeseken, F. Tellegen and P. C. Henriquez, *Rec. trav. chim.*, **50**, 909 (1931).

(6) J. Boeseken, F. Tellegen and P. C. Henriquez, *This Journal*, **55**, 1284 (1933).

the preparations involved not only a high reaction temperature but also a fractional distillation at temperatures above 100°.

The isomerization of the less stable 53° isomer is also brought about by catalytic amounts of aluminum chloride in benzene solution at room temperature or by refluxing with thionyl chloride.<sup>7</sup> When *trans*-2,3-dichloro-*p*-dioxane was treated with thionyl chloride for the same length of time, none of the 53° isomer was found, showing that the equilibrium is completely on the side of the 31° form.

The instability of the 53° isomer raised questions concerning the results of early experiments on the addition of chlorine to dioxene,<sup>8</sup> as failure to detect the then unknown 53° isomer might have been due to isomerization during the purification process. When the experiment was repeated under conditions not conducive to isomerization, both isomers were found, the 53° isomer predominating.

With both isomers at hand, we wished to make a definite assignment of configuration. The *trans* structure of the 31° isomer was indicated by its lower boiling point and its greater stability.<sup>9</sup>

To confirm this assignment of configuration, we treated *p*-dioxene with iodobenzene dichloride. This reagent is reputed to give only *cis* products when employed under anhydrous conditions.<sup>10,11</sup> However, when *p*-dioxene was treated with iodobenzene dichloride in carbon tetrachloride solution, the *trans/cis* isomer ratio of the product was about 20:1, as determined by infrared spectroscopy.

Because of this conflicting evidence we decided to attempt a kinetic resolution according to the method of Lucas and Gould<sup>12</sup> which has been used more recently by Cristol and co-workers.<sup>13,14</sup> This method is applicable if the two component stereoisomers of the racemic-*trans* form react at different rates with an optically active base, in this case brucine. Using less than the stoichiometric amount of the base should render the unreacted fraction of the compound enriched with the more slowly reacting stereoisomer and thus optically active. We obtained a specific rotation of  $[\alpha]^{25D} -36^\circ$  with the 31° isomer. The absence of brucine, which rotates in the same direction, was clearly demonstrated by the fact that the infrared spectrum of the active material was identical with that of a pure, non-active sample. None of the brucine absorption bands were detectable. Furthermore, optically active 2,3-dichloro-*p*-dioxane should lose its activity on hydrolysis because of the destruction of the centers of asymmetry, and this was found to be the case. The *trans* configuration of the 31° isomer being now clearly established, the *cis* configuration must be assigned to the 53° isomer.

(7) Adapted from a procedure used by M. Cooper, Ph.D. Dissertation, Northwestern University, 1955, to isomerize tetrachlorodioxanes.

(8) R. K. Summerbell and L. N. Bauer, *THIS JOURNAL*, **57**, 2364 (1935).

(9) R. K. Summerbell and Gregory J. Lestina, *ibid.*, **79**, 3878 (1957).

(10) J. Decombe and J. Rabinovitch, *Compt. rend.*, **225**, 583 (1947).

(11) D. H. R. Barton and E. Miller, *THIS JOURNAL*, **72**, 370 (1950).

(12) H. J. Lucas and C. W. Gould, *ibid.*, **64**, 601 (1942).

(13) S. J. Cristol, *ibid.*, **71**, 1894 (1949).

(14) S. J. Cristol, F. R. Stermitz and P. S. Ramey, *ibid.*, **78**, 4939 (1956).

Since the resolution is an absolute proof, it must be concluded that the addition of chlorine by means of iodobenzene dichloride occurred in an almost exclusively *trans* manner. This is even more surprising considering the predominant formation of *cis*-2,3-dichloro-*p*-dioxane from *p*-dioxene and molecular chlorine. Cristol and co-workers<sup>14</sup> have observed a similar case. When they treated acenaphthylene with iodobenzene dichloride, preferably in the presence of trinitrobenzene, the product isolated was *trans*-1,2-dichloroacenaphthene, whereas the addition of molecular chlorine to acenaphthylene resulted in the formation of the *cis* compound. However, the yields were low. We used infrared spectroscopy to determine the ratio of *cis*- and *trans*-2,3-dichlorodioxanes and found that iodobenzene dichloride produced over 90% of the *trans* isomer, whereas molecular chlorine gave about 60% *cis* and 40% *trans* compound. It is concluded that the *cis* addition of chlorine by means of iodobenzene dichloride is not a general phenomenon.<sup>11</sup> In our case iodobenzene dichloride, in contrast to molecular chlorine, proved to be a reagent for almost exclusive *trans* addition. Obviously, neither of the mechanisms proposed by Barton and Miller<sup>11</sup> can account for this.

The products from the reactions of the new isomer are, as far as investigated, the same as those from the *trans* isomer, which is to be expected if a carbonium ion mechanism is involved: *cis*-2,3-dichloro-*p*-dioxane reacts with phenylmagnesium bromide to give 2,3-diphenyl-*p*-dioxane<sup>15</sup> and with ethylene glycol to form the same mixture of *trans*-1,4,5,8-tetraoxadecalin and bi-1,3-dioxacyclopentyl as reported for the *trans* isomer.<sup>5,16</sup> The reaction with silver acetate has already been mentioned.

However, there are considerable differences in the rates of the reactions of the two isomers. As a typical example amenable to convenient study we have chosen the hydrolysis of the 2,3-dichloro-*p*-dioxanes. Salomaa,<sup>17</sup> who has investigated the kinetics of this reaction extensively with the *trans* isomer, using a titrimetric procedure, found it to be a first-order reaction and presented evidence for a carbonium ion intermediate. Using conductivity measurements to follow the course of the reaction, we obtained a rate constant of  $4.03 \times 10^{-4} \text{ sec.}^{-1}$  for the hydrolysis of the *trans* isomer in 50% aqueous dioxane at 25.1°, which is in good agreement with the reported data.<sup>17</sup>

#### HYDROLYSIS OF THE *cis* ISOMER IN 50% AQUEOUS DIOXANE

Temp., °C.	Rate const. $\times 10^3$	$k_{\text{aver.}} \times 10^3$
19.7	2.99	
19.7	3.09	3.04
25.1	5.51	
25.1	5.57	5.54
30.1	9.39	
30.1	9.37	9.38

It is seen that at 25° the *cis* isomer hydrolyzes fourteen times as fast as the *trans* isomer. The activation energy calculated for the *cis* compound

(15) R. K. Summerbell and R. Christ, *ibid.*, **54**, 3777 (1932).

(16) O. Hassel and Chr. Rømming, *Acta Chem. Scand.*, **10**, 136 (1956).

(17) Pentti Salomaa, *ibid.*, **8**, 744 (1954).

was 19,900 cal., compared with 21,310 for the *trans* isomer.<sup>17</sup> Since optically active *trans*-2,3-dichlorodioxane was available from the resolution with brucine, we also followed the hydrolysis reaction by observing the loss of rotation. The observed polarimetric rate of  $5.5 \times 10^{-4}$  sec.<sup>-1</sup> for the hydrolysis in 50% aqueous dioxane at 25.2° differs from the conductometric and titrimetric rates by a factor of 1.35. This indicates that the destruction of the asymmetric centers by hydrolysis is not the only cause for the loss of activity and that racemization must occur simultaneously.

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### Experimental

**Preparation of 2-Chloro-*p*-dioxene.**—A solution of 157 g. (1 mole) of 2,3-dichloro-*p*-dioxane and 149 g. of freshly distilled dimethylaniline was heated rapidly to 180°, after which the temperature was raised slowly. At approximately 200° the mixture suddenly turned dark and started to boil. The heat was immediately turned off, and the exothermic reaction caused a fast distillation which only at the end needed further heat input. A colorless distillate boiling at 140–160° was obtained in a yield of 85 g. The product was redistilled under reduced pressure and gave 55 g. (46%) of pure material, b.p. 38–39° (12 mm.),  $n_D^{20}$  1.4685.

*Anal.* Calcd. for C<sub>4</sub>H<sub>8</sub>O<sub>2</sub>Cl: C, 39.86; H, 4.18. Found: C, 40.03; H, 4.06.

**Preparation of 2,2-Dichloro-*p*-dioxane.**—2-Chloro-*p*-dioxene (43 g., 0.36 mole) was dissolved in 50 ml. of chloroform and cooled to -5° in an ice-salt-bath. A stream of dry hydrogen chloride was passed in at a rate of 5 mmoles/minute. After 2.5 hr., a drop of the temperature in the flask indicated that the addition reaction was complete. Nitrogen was bubbled through for 1 hr., then the solvent was evaporated under reduced pressure. Distillation of the residue through a 10-inch glass-packed column gave 31.8 g. (57%) of a colorless liquid, boiling 45–50° (4 mm.), on redistillation 33–35° (0.5 mm.),  $n_D^{20}$  1.4797.

*Anal.* Calcd. for C<sub>4</sub>H<sub>8</sub>Cl<sub>2</sub>: C, 30.60; H, 3.85. Found: C, 30.98; H, 3.51.

The compound is unstable and tends to eliminate hydrogen chloride even at room temperature.

**Hydrolysis of 2,2-Dichloro-*p*-dioxane.**—On the steam-bath, 5 g. of 2,2-dichloro-*p*-dioxane and 30 ml. of water were heated until most of the water was evaporated. The viscous residue solidified after distillation *in vacuo*. Since the melting point of *p*-dioxanone is not characteristic because of its tendency to polymerize, the infrared spectrum of the hydrolysis product was taken in carbon tetrachloride solution. It was identical with the spectrum of an authentic sample of *p*-dioxanone.

**Reaction with Phenylmagnesium Bromide.**—A Grignard solution was prepared by treating 1.6 g. of magnesium with 10 g. (0.064 mole) of phenyl bromide in 30 ml. of ether. To this a solution of 5 g. (0.032 mole) of 2,2-dichloro-*p*-dioxane in 20 ml. of ether was added slowly. After completion of the addition, the solution was stirred for an additional 30 minutes and then poured on a mixture of 20 ml. of a 10% ammonium chloride solution and 50 g. of ice. There was formed a precipitate which was brought into solution by addition of 100 ml. of ether. The ether layer was separated and dried with calcium chloride. Evaporation of the ether left 4.3 g. (57%) of a solid product, which was recrystallized from *n*-hexane with use of Norite and dried in a drying pistol at 56° under vacuum. The m.p. of the product (119–120°) was not depressed by admixture of a sample of 2,2-diphenyl-*p*-dioxane from another preparation<sup>4</sup> (reaction of *p*-dioxanone with phenylmagnesium bromide and ring closure with HCl).

**Preparation of *cis*-2,3-Dichloro-*p*-dioxane.**—A solution of 50 ml. of *p*-dioxane and 50 ml. of carbon tetrachloride was brought to reflux and chlorine was introduced at a rate of 6 mmoles/minute for 4 hr. The temperature in the flask was 83° at the beginning and 90° at the end of the chlorination. Hydrogen chloride and excess chlorine were expelled by bubbling nitrogen through the mixture. Then the sol-

vent was evaporated under reduced pressure and 50 ml. of a 2:1 pentane-ether mixture was added. On standing in an ice-salt-bath, crystallization occurred, yielding 23 g. (25%) of material, m.p. 53°, after recrystallization from pentane-ether. The yield can be increased if the chlorination product is directly subjected to a fractional distillation at low temperatures under reduced pressure (1 mm.), collecting the higher boiling fractions which are mixtures of *cis*- and *trans*-2,3-dichloro-*p*-dioxane enriched with the *cis* isomer. They may then be recrystallized from ether-pentane. However, since the preparation is very easy and the starting materials are readily available, the tedious distillation usually was omitted and lower yields were accepted.

*Anal.* Calcd. for C<sub>4</sub>H<sub>8</sub>O<sub>2</sub>Cl<sub>2</sub>: C, 30.60; H, 3.85. Found: C, 30.53; H, 3.81.

**Hydrolysis of *cis*-2,3-Dichloro-*p*-dioxane.**—To 0.157 g. (1.00 mmole) of *cis*-2,3-dichloro-*p*-dioxane, 40 ml. of water was added and the mixture was heated for 1 hr. on the steam-bath. To the hydrolysate was added a solution of 0.400 g. (2.1 mmoles) of *p*-nitrophenylhydrazine hydrochloride in 10 ml. of water. The precipitate was allowed to stand for 1 hr., filtered through a weighed sintered glass crucible, washed several times with dilute hydrochloric acid and dried for 12 hr. at 110°; expected yield for *p*-nitrophenyl osazone of glyoxal: 0.329 g.; weight of dried product: 0.320 g. This corresponds to a yield of 97.3%. The compound melted at 305–310° with decomposition (reported 311°).

In another experiment the hydrolysate was made alkaline. The equivalent amount of benzoyl chloride was added portionwise, and the mixture was shaken after each addition until the smell of benzoyl chloride disappeared. The product was filtered and recrystallized from methanol to give material melting at 71–72°. A mixed melting point with an authentic sample of ethylene glycol dibenzoate showed no depression.

**Reaction of *cis*-2,3-Dichloro-*p*-dioxane with Silver Acetate.**—A mixture of *cis*-2,3-dichloro-*p*-dioxane (5 g., 0.032 mole), silver acetate (11 g., 0.066 mole) and benzene (250 ml.) was placed in a flask and shaken for 24 hr. at room temperature. The silver chloride was filtered off and the benzene was evaporated under reduced pressure. Recrystallization of the residue from ether gave 5.1 g. (79%) of colorless crystals, m.p. 104–105°. Admixture of an authentic sample of 2,3-*p*-dioxanediol diacetate<sup>9</sup> effected no depression of the melting point. The infrared spectra were identical.

**Method of Determining the Relative Amounts of *cis*- and *trans*-2,3-Dichloro-*p*-dioxane in Mixtures by Infrared Analysis.**—The procedure of Zimmerman<sup>18</sup> was employed, using the peaks at 10.55  $\mu$  (*cis* isomer) and 11.42  $\mu$  (*trans* isomer). The calculations were checked by making up a series of knowns, and good agreement was observed. Carbon disulfide was mostly used as solvent, but carbon tetrachloride also was found suitable.

**Chlorination of *p*-Dioxane without Solvent.**—Dry chlorine was introduced into *p*-dioxane (88 g., 1 mole) at a rate of 4 mmoles/minute, at first at room temperature, but since apparently no reaction occurred at this temperature (yellow color of the solution, no heat of reaction), the mixture was heated to 70°. The reaction started with disappearance of the yellow color and an increase in temperature. The heat was turned off and the rate of chlorine input was regulated so that the temperature remained constant at about 70°. Samples of 10 ml. were taken at approximately 25, 35 and 55% completion of the reaction. They were pipetted into small flasks, freed from chlorine by bubbling nitrogen through, and distilled at 0.05 mm. pressure, keeping the bath temperature below 70°. The following results were obtained:

	Time of chlorination, hr.	Weight of dichloro- <i>p</i> -dioxane fraction, g.	Ratio <i>cis/trans</i>
1	2	4.8	42/58
2	4	5.9	40/60
3	6	9.2	41/59

The chlorination was stopped and the mixture was heated to 110°. After 3 hr. the ratio *cis/trans* was found to be 18/82; after 6 hr., 11/89. Then the mixture was heated to

(18) H. E. Zimmerman, *THIS JOURNAL*, **78**, 1172 (1956).

130° for 3 hr., which resulted in a decrease of the *cis* isomer to less than 5%.

**Isomerization Reactions.**—*cis*-2,3-Dichloro-*p*-dioxane (1 g.) was dissolved in 25 ml. of a saturated solution of aluminum chloride in benzene and allowed to stand at room temperature for two days. Pentane (50 ml.) was added to precipitate the aluminum chloride. The solution was decanted and the solvent was evaporated under reduced pressure. Infrared analysis showed that complete isomerization to the *trans* isomer had occurred.

A solution of 3 g. of *cis*-2,3-dichloro-*p*-dioxane in 50 ml. of thionyl chloride was refluxed for 24 hr. After removal of the thionyl chloride by distillation under vacuum, the residue was distilled at 1 mm. pressure. The recovered material (2.1 g.) was a mixture of 94% *trans* and 6% *cis* isomer, determined by infrared analysis. The liquid product solidified on cooling and melted at 28–30° after recrystallization from pentane. When *trans*-2,3-dichloro-*p*-dioxane was refluxed for 24 hr. with thionyl chloride, none of the *cis* isomer was detectable in the infrared spectrum of the product.

**Addition of Chlorine to *p*-Dioxane.**—*p*-Dioxane was freed from peroxides by the method of Dasler and Bauer.<sup>19</sup> The material was finally distilled over sodium and had a boiling point of 94–94.5°. A solution of 4.3 g. (0.05 mole) of *p*-dioxane in 50 ml. of carbon tetrachloride was cooled to –15° in an ice-salt-bath, and chlorine was introduced at a rate of 3 mmoles/minute. After 20 minutes the solution turned yellow, indicating that the addition was finished. Dry nitrogen was bubbled through for 20 minutes to displace excess chlorine. Infrared analysis showed that the product was a mixture of 61% *cis*- and 39% *trans*-2,3-dichloro-*p*-dioxane. The solvent was evaporated, and the residue was brought to partial crystallization by cooling. The product was recrystallized from pentane (1.6 g., m.p. 49–51°).

**Reaction of *p*-Dioxane with Iodobenzene Dichloride.**—Iodobenzene dichloride (2.75 g., 0.01 mole) was added to a solution of 0.8 ml. (0.01 mole) of peroxide-free *p*-dioxane in dry carbon tetrachloride. The mixture was heated slowly to the boiling point and refluxed for 1 hr., during which time the crystals of iodobenzene dichloride dissolved. Since a separation of the products (2,3-dichloro-*p*-dioxane and iodobenzene) by distillation did not appear promising because of the close boiling points and since it had been found that iodobenzene did not absorb at the wave lengths used for the determination of the isomer ratio, the reaction mixture was used for the infrared analysis without separation. The product was composed of 95% of the *trans* isomer and 5% of the *cis* isomer. To decrease the possibility of isomerization, the experiment was repeated at room temperature, allowing the mixture to stand overnight and heating it to only 40° for 5 additional hr. The results were the same. It was determined also that *cis*-2,3-dichloro-*p*-dioxane was not isomerized when it was refluxed in carbon tetrachloride for several hours in presence of iodobenzene dichloride.

**Resolution of *trans*-2,3-Dichloro-*p*-dioxane.**—Numerous experiments were carried out with a variety of solvents, at different temperatures and with different reaction times. Some did not give resolution at all, and some gave only a slightly active compound. The best results were obtained under the conditions described below.

A mixture of 15 g. (0.038 mole) of brucine, 8 g. (0.051 mole) of *trans*-2,3-dichlorodioxane, m.p. 31°, and 100 ml. of carbon tetrachloride was heated to 60° for 8 days. The solid was filtered off and the solvent was evaporated under reduced pressure. The ether extract of the residue was washed consecutively three times with 30 ml. of 1 *N* hydrochloric acid, once with 30 ml. of saturated sodium bicarbonate solution and dried over sodium sulfate. After evapora-

tion of the solvent, the residue was dissolved in pentane and crystallized by cooling to –30°. There was obtained 2.4 g. of *trans*-2,3-dichloro-*p*-dioxane, m.p. 28–30°. The absence of brucine was shown by a negative test with concentrated nitric acid<sup>20</sup> and by the absence of brucine bands in the infrared spectrum. Specific rotation in chloroform solution was –36°, measured at 25° in a 2-dm. polarimeter tube and in a concentration of 0.1 g./ml.

When *cis*-2,3-dichloro-*p*-dioxane, m.p. 53°, was treated with brucine as described above, a slight rotation was obtained. However, the infrared spectrum showed that the compound had undergone considerable isomerization to the *trans* isomer. The rotation is attributed to the partially resolved isomerization product. The optically active *trans* isomer from the previous experiment did not contain any detectable amount (<1%) of the *cis* isomer. Hydrolysis of the optically active compound in 50% aqueous dioxane resulted in complete loss of rotation.

**Reaction of *cis*-2,3-Dichloro-*p*-dioxane with Phenylmagnesium Bromide.**—A Grignard solution was prepared from 1.6 g. of magnesium and 10 g. (0.064 mole) of bromobenzene. To this was added a solution of 5 g. (0.032 mole) of *cis*-2,3-dichloro-*p*-dioxane in 20 ml. of ether. After 20 minutes of additional stirring the mixture was poured on an ammonium chloride solution mixed with ice. Crystallization occurred only after the product had been distilled *in vacuo*, yielding 1.7 g. (20%) of 2,3-diphenyl-*p*-dioxane, m.p. 46–48°. Its identity was established by mixed melting point with an authentic sample of 2,3-diphenyl-*p*-dioxane and comparison of the infrared spectra.

**Reaction of *cis*-2,3-Dichloro-*p*-dioxane with Ethylene Glycol.**—*cis*-2,3-Dichloro-*p*-dioxane (7.8 g., 0.05 mole) and a slight excess of ethylene glycol were refluxed in benzene solution until the development of hydrogen chloride ceased. The benzene layer was separated and the solvent was evaporated under vacuum, yielding 2.1 g. (29%) of material, m.p. 90–110°. The infrared spectrum of this crude product was identical with that of the mixture of bi-1,3-dioxacyclopentyl and *trans*-1,4,5,8-tetraoxadecalin ("trans-1,4,5,8-naphthodioxane") obtained from the reaction of *trans*-2,3-dichloro-*p*-dioxane with ethylene glycol. When the reaction was carried out in presence of pyridine according to the method of Faass and Hilgert,<sup>21</sup> the only product isolated from both isomers was *trans*-1,4,5,8-tetraoxadecalin.

**Kinetics of the Hydrolysis of 2,3-Dichloro-*p*-dioxane.**—*p*-Dioxane was purified by the method of Hess and Frahm.<sup>22</sup> Into one arm of a Y-tube was pipetted 20 ml. of a 0.1 molar solution of 2,3-dichloro-*p*-dioxane in dioxane, the other arm of the tube was filled with 20 ml. of distilled water. After thermal equilibration in a thermostat, the contents of both arms of the Y-tube were brought together, mixed well and placed in a conductivity cell with platinum electrodes. The resistance was measured with a Wheatstone bridge at appropriate intervals, and the rate constants were determined graphically by plotting  $\log R/(R - R_{\infty})$  versus time. The activation energy for the hydrolysis of *cis*-2,3-dichloro-*p*-dioxane was also determined graphically from the slope of a plot of  $\log K$  vs.  $1/T$ .

The loss of activity of optically active *trans*-2,3-dichloro-*p*-dioxane during hydrolysis was observed in a thermostated 2-dm. polarimeter tube. A 0.11 molar concentration of the compound in 50% aqueous dioxane was used, giving an initial rotation of –1.23°, and readings were taken at intervals of 1 minute. The calculated rate constants of two separate runs were in good agreement with each other.

#### EVANSTON, ILLINOIS

(20) R. Kersting, *Ann.*, **125**, 254 (1863).

(21) U. Faass and H. Hilgert, *Chem. Ber.*, **87**, 1343 (1954).

(22) K. Hess and H. Frahm, *Ber.*, **71**, 2627 (1938).

(19) W. Dasler and C. W. Bauer, *Ind. Eng. Chem., Anal. Ed.*, **18**, 52 (1946).