enesulfonic acid, 4 ml. of water and 1 ml. of 1% potassium persulfate solution. After polymerization, 15.08 ml. of 6.07 *N* sodium hydroxide was required for neutralization, the calculated quantity being 15.25 ml. The yield of polymer was 7.5 g., a conversion of 62%, with a specific viscosity of 0.988.

Effect of Conditions on Polymerization of Ethylenesulfonic Acid.—Experiments were run and the polymers were isolated as described above. A 50% ethylenesulfonic acid solution with 0.1% hydrogen peroxide as catalyst gave a 44% conversion to polymer in 16 hours at 55°, the specific viscosity of a 1% solution in water being 0.466.

A 50% ethylenesulfonic acid solution with 0.1% potassium persulfate gave a 22% conversion to polymer in 15 hours at room temperature, the specific viscosity being 1.162.

A 75% ethylenesulfonic acid solution irradiated with an ultraviolet lamp gave a 73% conversion to polymer in 16 hours at 0°, the specific viscosity being 5.613. This polymer was estimated to have a weight-average molecular weight of about 250,000.

Polyethylenesulfonic Acid.—A solution of 156 g. of sodium polyethylenesulfonate (having a specific viscosity of 0.675 in a 1% aqueous solution) in 400 ml. of water was chilled in ice and saturated with hydrogen chloride. The precipitate of sodium chloride was filtered off and was washed with 50 ml. of cold, concentrated hydrochloric acid. The combined filtrates were evaporated to dryness on a steam-bath *in vacuo*. Water was added and distilled off until the distillate gave a negative test for chloride ion, the final distillation not being carried to completion. The resulting reddish-brown, viscous solution contained 46.3% polymer, and sodium analysis indicated that the conversion to free acid was 98% complete. Evaporation of a portion of this solution on a glass plate yielded a brittle, very hygroscopic film of polyethylenesulfonic acid.

Copolymerization of Methyl Acrylate and Ethylenesulfonic Acid.—A solution of 1 g. (0.0093 mole) of ethylenesulfonic acid in 3 g. (0.035 mole) of methyl acrylate was irradiated *in vacuo* with a Hanovia EH-4 lamp for 48 hours. The resulting hard, dark brown copolymer was dissolved in 300 ml. of 1% sodium hydroxide and the clear, tan, viscous solution obtained was added to 800 ml. of methanol. The white, rubbery copolymer was purified by solution in water and precipitation with methanol. A hard, white solid (1.7 g.) was obtained after drying *in vacuo* at 80°. It contained 2.9% sulfur, equivalent to 11.8% sodium ethylenesulfonate.

Repetition of the experiment with 4 ml. of dioxane as solvent yielded 2.3 g. of rubbery polymer, isolated by solution in dioxane and precipitation with isopropyl alcohol. The copolymer contained 2.5% sulfur, equivalent to 8.5% ethylenesulfonic acid. It was soluble in aqueous alkali but precipitated on acidification. With equimolar quantities of ethylenesulfonic acid and methyl acrylate and dioxane as a solvent, a copolymer was obtained containing 4.1% sulfur, equivalent to 14.8% ethylenesulfonic acid.

Copolymerization of Acrylonitrile and Ethylenesulfonic Acid.—The procedure described for methyl acrylate was used; 1.06 g. (0.02 mole) of acrylonitrile and 2.16 g. (0.02 mole) of ethylenesulfonic acid dissolved in 4 ml. of dioxane yielded 0.2 g. of copolymer in 24 hours. The insoluble polymer was filtered and washed thoroughly with methanol. It contained 5.21% sulfur, equivalent to 17.6% ethylenesulfonic acid. The copolymer was highly swollen in water, but the gel was broken by the addition of sodium hydroxide. Substituting dimethylformamide for dioxane and irradiating for four days yielded 0.9 g. of hard, white copolymer after precipitation with methanol. This contained 5.85% sulfur, equivalent to 19.7% ethylenesulfonic acid; the specific viscosity of a 1% solution in dimethylformamide was 5.46.

WILMINGTON, DELAWARE

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

The Stereochemistry of Several 2,5-Disubstituted Dioxanes

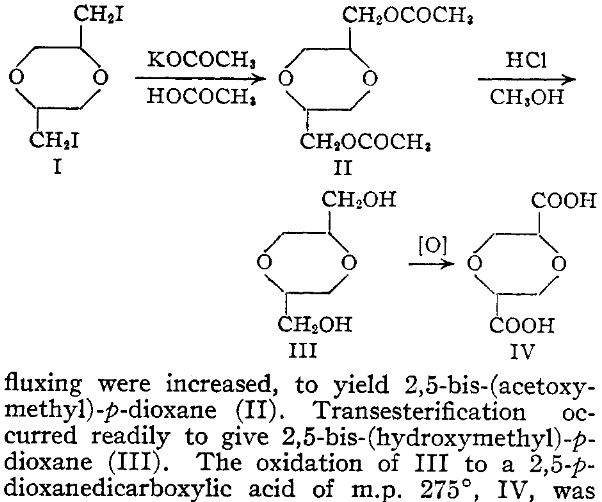
BY ROBERT K. SUMMERBELL AND JAMES R. STEPHENS

RECEIVED JUNE 30, 1954

"Diepiiodohydrin" has previously been shown to be 2,5-bis-(iodomethyl)-*p*-dioxane (I), but the configuration of no 2,5-derivative of dioxane is known. I was converted to the dicarboxylic acid of the same number of carbon atoms which in turn was isomerized by strong alkali to a different acid. The latter was shown to be *cis* by a partial resolution with brucine and by its formation from the hydrolysis of a monomeric anhydride. The *cis*-acid was reduced to the glycol which in turn was converted through the tosylate to *cis*-2,5-bis-(iodomethyl)-*p*-dioxane, a different compound from "diepiiodohydrin." The latter must therefore be *trans*. The *trans*-acid was shown to be the statistically preferred form by partial equilibration with alkali. Also the *trans* forms of the 2,5-series are uniformly higher melting than the corresponding *cis* compounds. Both properties are consistent with the equatorial–polar (axial) concept. A number of venerable glycerol derivatives have been assigned definite structures and configurations.

In a previous paper we have shown[1] the configurations of several key derivatives of 2,6-disubstituted *p*-dioxanes and established that "diepiiodohydrin" (I) is one form of 2,5-bis-(iodomethyl)-*p*-dioxane. This compound then afforded an entry into the study of the stereochemistry of 2,5-disubstituted *p*-dioxanes.

As a step toward the elucidation of the geometry of I, we attempted to convert it to a 2,5-*p*-dioxanedicarboxylic acid of the same configuration. This was accomplished by the following sequence of reactions.



The initial step in this series occasioned some difficulty, a low yield of 2-acetoxymethyl-5-iodomethyl-*p*-dioxane being the only isolated product under the mild conditions first employed. The second iodine atom was replaced readily when the proportion of potassium acetate and time of refluxing were increased, to yield 2,5-bis-(acetoxymethyl)-*p*-dioxane (II). Transesterification occurred readily to give 2,5-bis-(hydroxymethyl)-*p*-dioxane (III). The oxidation of III to a 2,5-*p*-dioxanedicarboxylic acid of m.p. 275°, IV, was accomplished by a variety of reagents. Potassium

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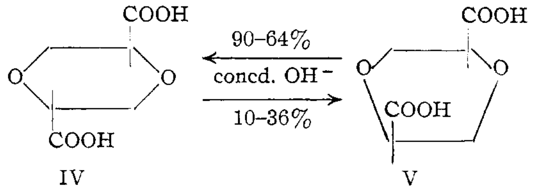
[1] R. K. Summerbell and J. R. Stephens, THIS JOURNAL, **76**, 731 (1954).

permanganate in dilute base was first used, but the reaction was somewhat difficult to control and the presence of hydroxyl ion which might isomerize the product acid was undesirable.

Marckwald[2] used potassium dichromate in dilute sulfuric acid to convert optically pure *d*-2-methyl-1-butanol to optically pure *d*-2-methyl-1-butanoic acid. We found that his reagent converted III to IV under milder conditions than he used. Since non-racemization in Marckwald's case is equivalent to non-isomerization in ours, it was concluded that III and IV have the same configuration. The best conversion of III to IV was accomplished by the use of hot concentrated nitric acid. This reagent also will oxidize I directly to IV but in poor yield.

The geometrical isomer of IV was first obtained by the action of hot 22% potassium hydroxide on IV, followed by acidification. This new acid of m.p. 178°, V, was extremely soluble in cold water in marked contrast to IV which was practically insoluble in cold water. These widely different solubility characteristics of the acids afforded an easy separation. The fact that IV could be recovered quantitatively gave value to this equilibration as a preparative method for V even though the latter could only be obtained in about 10% yield. The reverse reaction, the isomerization of V to IV, was readily accomplished under identical conditions yielding 64% of IV, showing that IV is definitely the statistically preferred isomer and that the equilibrium is somewhere between 90 and 64% of IV.



Usually esters are preferred to acids for such isomerizations,[3] but in this case attempts to isomerize the ester in methanol using sodium methoxide as the equilibrating agent resulted in an intractable tar. Further work with the ester was not attempted when it was found that IV could be converted to V easily through the intermediates VIII, IX and X. No isomerization of IV or V could be detected when these compounds were subjected to boiling concentrated nitric or hydrochloric acids. The dimethyl esters VI and VII, of IV and V, respectively, were readily obtained and served as convenient derivatives, since mixtures of isomers showed typical melting point depressions.

By the use of brucine, V was partially resolved into an optical antimer, whereas no resolution could be accomplished with IV. V therefore was assigned the structure of racemic or *cis*-2,5-*p*-dioxanedicarboxylic acid, and IV was assigned the structure of *trans*-2,5-*p*-dioxanedicarboxylic acid as the only possible alternative.

Confirmation for these assignments was then sought by the hydrolysis of the monomeric anhydride of 2,5-*p*-dioxanedicarboxylic acid which from structural considerations could give only the *cis*-acid. This anhydride could be prepared from IV by three operations (Chart 1). IV when subjected to the action of boiling acetic anhydride yielded the mixed anhydride. This compound was established as *trans*-2,5-*p*-dioxanedicarboxylicdiacetic anhydride (VIII) by analysis, neutral equivalent and its hydrolysis to IV. It was remarkably stable for a mixed anhydride, subliming unchanged at 150° and 5 mm. When VIII was heated at atmospheric pressure it melted at 151° and then lost the elements of acetic anhydride at *ca.* 160° and resolidified. The new, white, brittle solid produced gave IV on hydrolysis and was presumably poly-*trans*-2,5-*p*-dioxanedicarboxylic anhydride IX. IX then was destructively distilled at reduced pressure. The distillate X, a low-melting solid, was purified and a molecular weight determination indicated it to be monomeric 2,5-*p*-dioxanedicarboxylic anhydride. The hydrolysis of X produced V. This then gave additional evidence that the original assignment of configurations to the acids was correct.

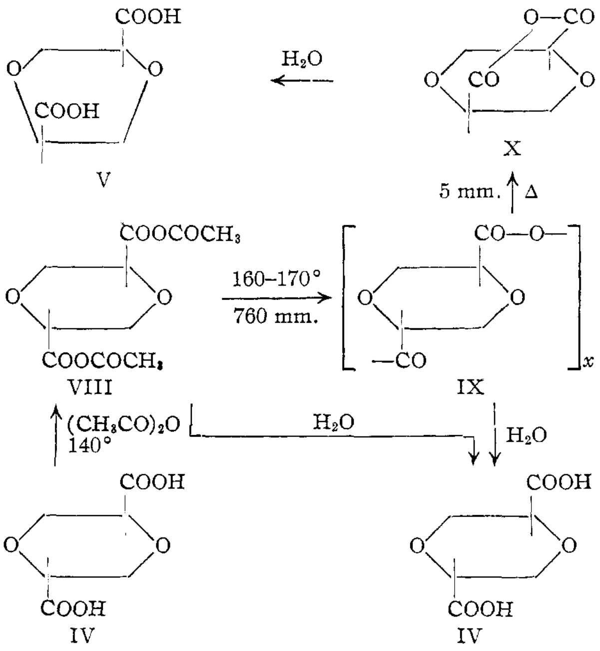


CHART 1

We already have cited evidence that III is of the same configuration as IV and, accordingly, III was assigned the configuration of *trans*-2,5-bis-(hydroxymethyl)-*p*-dioxane. I and II also are assigned the *trans* configuration, as the conversion of I to III *via* II should not affect orientation of the extra-nuclear methylene group relative to the dioxane ring.

To complete the set of 2,5- and 2,6-bis-(iodomethyl)-*p*-dioxanes,[1] the geometric isomer of I was prepared by a sequence of reactions that converted V or its ester VII to *cis*-2,5-bis-(iodomethyl)-*p*-dioxane (XIII) (Chart 2). Since the basic reagent lithium aluminum hydride was used in the first step in this sequence the same operations were carried out on *trans*-2,6-*p*-dioxanedicarboxylic acid

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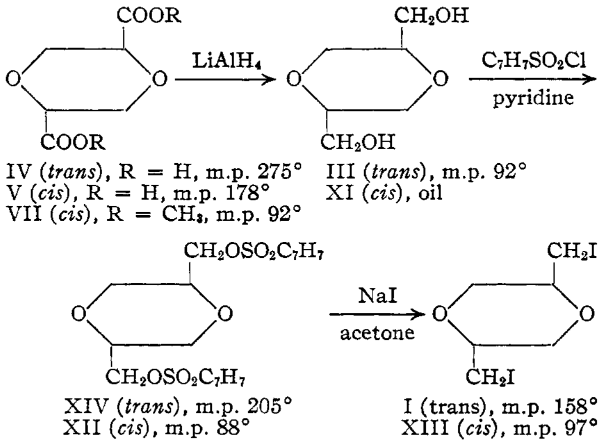
[2] W. Marckwald, *Ber.*, **37**, 1045 (1904).

[3] W. Hückel and E. Goth, *ibid.*, **58**, 447 (1925).

(IV) as a check on possible isomerization in that step. These latter operations produced a different sequence of isomers, and here the final product was identical with I. These sequences are consistent with the assignments of configuration made previously.



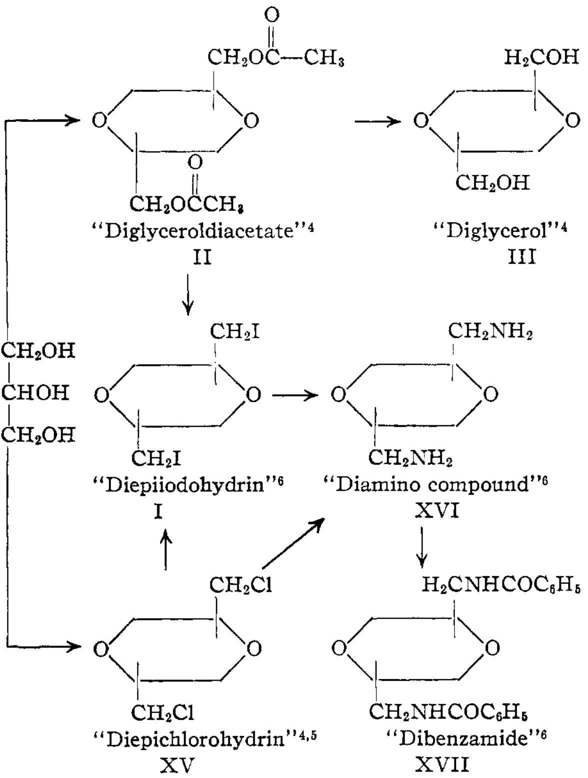
IV (*trans*), R = H, m.p. 275° III (*trans*), m.p. 92°
V (*cis*), R = H, m.p. 178° XI (*cis*), oil
VII (*cis*), R = CH$_3$, m.p. 92°

XIV (*trans*), m.p. 205° I (trans), m.p. 158°
XII (*cis*), m.p. 88° XIII (*cis*), m.p. 97°

CHART 2

For many years, certain glycerol derivatives have been assigned dioxane structures without experimental proof of their nature, and, of course, nothing was known of their configuration. They were obtained in small yields when glycerol was condensed with various reagents. Several of the compounds obtained in our work are identical with some that have been previously described. Thus "diglycerol diacetate," prepared by Battegay, Buser and Schlager[4] by the acid-catalyzed condensation of glycerol with acetic acid was *trans*-2,5-bis-(acetoxymethyl)-*p*-dioxane (II) and "diglycerol" obtained by them from the diacetate by a method essentially the same as that used by us was *trans*-2,5-bis-(hydroxymethyl)-*p*-dioxane (III). The "diepichlorohydrin" (XV), obtained by Fauconnier and Sanson[5] in 1887 by the action of hydrogen chloride at high temperatures on glycerol can now be designated as *trans*-2,5-bis-(chloromethyl)-*p*-dioxane, since Stoehr[6] has converted it to "diepiiodohydrin" (I) using potassium iodide in alcohol. By the action of concentrated aqueous ammonia in a sealed tube on "diepichlorohydrin" (and apparently under different conditions on diepiiodohydrin itself), Stoehr obtained a "diamino compound" XVI. He converted this amine to a dibenzamide XVII of the same melting point as the dibenzamide obtained by us in a similar series of reactions from *trans*-2,5-bis-(iodomethyl)-*p*-dioxane (I). Thus Stoehr's amine was *trans*-2,5-bis-(aminomethyl)-*p*-dioxane. It is curious that although Stoehr characterized this solid amine well, he did not record its melting point.

The configurations of these older glycerol derivatives are shown in Chart 3.



"Diglyceroldiacetate"[4] II
"Diglycerol"[4] III
"Diepiiodohydrin"[6] I
"Diamino compound"[6] XVI
"Diepichlorohydrin"[4,5] XV
"Dibenzamide"[6] XVII

CHART 3

All of the above compounds have a 2,5 structure and a *trans* configuration, but the initial glycerol condensations gave minute yields of the compounds reported. It is our opinion that several or all of the other possible isomers were probably present in these earlier preparations, but that only a small fraction of the least soluble and highest melting forms, the *trans*-2,5-derivatives, were isolated.

A different situation prevails concerning the bis-(nitratomercurimethyl)-*p*-dioxane and the bis-(halomercurimethyl)-*p*-dioxanes that were the precursors of I in our work. Since the methods of converting these compounds to I made use of mild conditions, these mercury compounds must also belong to the *trans*-2,5-series. In contrast to the compounds discussed in the previous paragraph, these mercury derivatives were obtained in excellent yields. Evidently the condensation involving allyl alcohol and mercuric salts is highly stereospecific. These mercury derivatives of hitherto ambiguous structures are being used in investigations of protein structure.[7] They should prove even more useful now that their structures and configurations are known.

We have applied already the equatorial–polar (axial) theory of Beckett, Pitzer and Spitzer[8] to the 2,6-disubstituted *p*-dioxanes. An inspection of the melting points of isomerides in a *cis–trans* pair of 2,5-disubstituted *p*-dioxanes shows the melting points of the *trans* isomers to be considerably higher than those of the *cis* isomers. This is opposite to the case of 2,6-derivatives where we have shown that the *cis*-2,6-isomers of a *cis–trans*

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[4] M. Battegay, H. Buser and E. Schlager, *Compt. rend.*, **188**, 796 (1929).

[5] M. Fauconnier and J. Sanson, *Bull. soc. chim.*, [2] **48**, 237 (1887).

[6] C. Stoehr, *J. prakt. Chem.*, [2] **55**, 78 (1887).

[7] J. T. Edsall, *Faraday Soc. Disc.*, **13**, 9 (1953); R. Straessle, THIS JOURNAL, **73**, 504 (1951).

[8] C. W. Beckett, K. S. Pitzer and R. Spitzer, Jr., *ibid.*, **69**, 2488 (1947).

pair are the higher melting isomers. As in the 2,6-case these facts again can be rationalized by imputing the higher melting point to the greater molecular symmetry of the diequatorial or dipolar (diaxial) configuration, which in the 2,5-series would be the *trans* compounds. Again it must be remembered that the melting points of the *cis* isomers are those of racemic material. We do not believe that the melting point of *d*- or *l*-*cis* 2,5-disubstituted *p*-dioxanes is higher than that of the isomeric *trans*(*meso*)-2,5-disubstituted *p*-dioxanes, but information concerning the actual experimental facts is not available at the present time. However, as an argument for the *trans*-2,5-configuration being the most stable form, it is seen that it is the statistically preferred configuration in an equilibration of *cis*- and *trans*-2,5-dioxanedicarboxylic acids by aqueous base.

Referring to the preparation of *trans*-2,5-bis-(iodomethyl)-*p*-dioxane from allyl alcohol it is seen that two molecules of allyl alcohol can be condensed by acidic mercuric nitrate solution theoretically to give four different isomers (the *cis* and *trans* forms of 2,5- and of 2,6-bis-(nitratomercurimethyl)-*p*-dioxane), yet we have obtained yields of at least 90% of *trans*-2,5-bis-(nitratomercurimethyl)-*p*-dioxane with no indication of the formation of another isomer. (The yield is probably very close to quantitative as this figure is based on the yield of I from allyl alcohol and there are the usual mechanical losses to be considered.) The cyclization of diallyl ether by aqueous mercuric acetate is not stereospecific as both forms of 2,6-bis-(acetatomercurimethyl)-*p*-dioxane are formed.[1] This difference in stereospecificity of different mercuric salts is being further investigated.

Four additional new compounds prepared in our work failed to give useful information as to the stereochemistry of 2,5-disubstituted *p*-dioxanes. These compounds are listed at the end of the Experimental section.

Experimental

***trans*-2,5-Bis-(iodomethyl)-*p*-dioxane (Diepiiodohydrin (I).**—This material can be prepared using the combined procedure of Biilmann[9] and Sand.[10] However, it was found expedient to modify this synthesis as follows: Four hundred and seventy grams (2.16 moles) of mercuric oxide were dissolved in 300 ml. of concd. nitric acid and 200 ml. of water. An additional 800 ml. of water was added and the solution was cooled to 0°. Then with stirring and cooling 300 ml. of allyl alcohol was added. Gradually a copious white precipitate formed. The mixture was left standing 6 hours. (Prolonged standing of the reaction mixture at this point may result in decomposition of the product.) The precipitate was filtered off and dissolved in 10% aqueous sodium hydroxide. Concentrated aqueous potassium iodide was then added until precipitation of *trans*-2,5-bis-(iodomercurimethyl)-*p*-dioxane was complete. It was filtered off and washed with water. The wet solid was refluxed with a solution of 700 g. of iodine, and 1000 g. of potassium iodide in 2500 ml. of water. (A flask large enough so that only about one-third of its volume is occupied by the reactants is recommended. Also a few ml. of benzene should be added to wash back iodine that sublimes out on the condenser.) Refluxing was continued until the organic mercury compound had all reacted (about 24 hours). The reaction mixture was cooled and *trans*-2,5-bis-(iodomethyl)-*p*-dioxane filtered and washed with dilute sodium bisulfite solution and then water. The dry solid was recrystallized from benzene yielding 344 g. (90%) of colorless crystals, m.p. 158°.[11]

***trans*-2,5-Bis-(acetoxymethyl)-*p*-dioxane (II).**—Eight hundred and fifty-four grams (8.72 moles) of fused potassium acetate was poured into a 5-liter flask. Three liters of glacial acetic acid and 468 g. (1.27 moles) of I were then added to the cooled contents of the flask. The mixture was heated just below the boiling point of the solution with little refluxing. After the reactants had dissolved, the solution was seeded with potassium iodide and heating was continued for nine days. One and a half liters of acetic acid was then removed by heating the mixture under reduced pressure. The residue was cooled to a semi-solid mass, and to it was added one liter of water. The undissolved solid product was filtered off. The filtrate was diluted with three times its volume of water and cooled to 0°. An additional amount of the brown solid precipitated which was added to the original yield. The entire yield was dissolved in boiling water, filtered from insoluble tars and cooled. Colorless crystals were obtained that melted at 124° and weighed 146 g. (50%). The mother liquor from recrystallization was evaporated and cooled to yield an additional 6 g. of product. (The melting point of this compound is the same as that reported by Battegay, *et al.*,[4] for "diglyceryl diacetate.")

***trans*-2,5-Bis-(hydroxymethyl)-*p*-dioxane (III).**—This compound, obtained by Battegay, *et al.*,[4] and formerly named "diglycerol," was synthesized as: A mixture of 144 g. (0.62 mole) of *trans*-2,5-bis-(acetoxymethyl)-*p*-dioxane and 600 ml. of a 3% solution of hydrogen chloride in methanol was refluxed one hour. The resulting solution was concentrated to one-half of its volume by distillation, then evaporated at reduced pressure until most of the reaction mixture solidified. The filtered solid was triturated with a benzene–isopropyl alcohol solution to yield 75.3 g. (82%) of *trans*-2,5-bis-(hydroxymethyl)-*p*-dioxane of m.p. 90°. Recrystallization from benzene–isopropyl alcohol solution raised the m.p to 92°.

Further evaporation of the methanolic mother liquor afforded an additional 15.5 g. of the glycol that melted at 85–88°.

Anal. Calcd. for $C_6H_{12}O_4$: C, 48.64; H, 8.16. Found: C, 48.94; H, 8.19.

***trans*-2,5-*p*-Dioxanedicarboxylic Acid (IV). A. From III Using Acidic Dichromate.**—To a solution consisting of 3.33 g. of potassium dichromate, 42 ml. of water and 4.45 g. of concentrated sulfuric acid was added 0.43 g. (0.0029 mole) of *trans*-2,5-bis-(hydroxymethyl)-*p*-dioxane. The solution was heated 15 minutes at 85°, then cooled to 0°. The precipitate was filtered off and washed with cold water. The colorless hydrated crystals obtained lost water without decomposition at 100° and then melted with decomposition at 275°. The yield was 0.36 g. (63.0%).

Anal. Calcd. for the hydrate $C_4H_8O_2(COOH)_2{\cdot}H_2O$: loss in weight at 100°, 9.29; neut. equiv., 97.1. Found: loss in weight at 100°, 9.43; neut. equiv., 98.2. Calcd. for the anhydrous acid $C_6H_8O_6$: C, 40.91; H,4.58; neut. equiv., 88.1. Found: C, 41.17; H, 4.85; neut. equiv., 88.4.

B. From III Using Concd. Nitric Acid.—Forty-seven and six-tenths grams (0.32 mole) of *trans*-2,5-bis-(hydroxymethyl)-*p*-dioxane in a five-liter flask was dissolved by the addition of 250 ml. of water and 665 ml. of concd. (sp. gr. 1.42) nitric acid. A few boiling chips were added to the contents of the flask which was heated on a steam-bath in a well-ventilated hood. When a vigorous reaction took place, heating was discontinued until the evolution of nitrogen dioxide subsided. It was again heated for 100 minutes, then cooled to 5° and the precipitated acid filtered off and washed with cold water. The acid after drying overnight at 45° weighed 57.2 g. (92%), and melted at 275°. The melting point was undepressed by admixture with the product of the preceding experiment.

C. From I and Concd. Nitric Acid.—A mixture of 3 g. (0.0081 mole) of *trans*-2,5-bis-(iodomethyl)-*p*-dioxane and 30 ml. of concd. (sp. gr. 1.42) nitric acid was placed in a beaker and heated on a steam-bath. The iodide went into solution with the evolution of iodine and nitrogen dioxide. Upon cooling the solution the organic acid precipitated. It was washed with cold water and dried to constant weight. In this manner 0.45 g. (28%) of *trans*-2,5-dioxanedicarboxylic acid monohydrate, m.p. 275°, was obtained.

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[9] E. Biilmann, *Ber.*, **33**, 2910 (1900).

[10] J. Sand, *ibid.*, **34**, 1394 (1901); R. R. Umhoefer, M.S. Thesis, Northwestern University, 1936, p. 13.

[11] All melting points were taken on a Fisher–Johns block.

The Preparation of *cis*-2,5-*p*-Dioxanedicarboxylic Acid (V). The Equilibration of the 2,5-*p*-Dioxanedicarboxylic Acids IV and V. A. IV to V.—Eighty-seven and seventenths grams (0.45 mole) of *trans*-2,5-*p*-dioxanedicarboxylic acid monohydrate was dissolved with heating in a solution of 635 g. of potassium hydroxide and 2250 ml. of water (22% KOH). The solution was heated on a steam-bath for 24 hours. It was then made acidic with concd. hydrochloric acid, cooled to 5°, and 71.4 g. of precipitated unchanged starting material filtered off. The filtrate was evaporated to dryness in a large shallow dish and the residue extracted with 2.5 kg. of boiling acetone in five portions. The acetone extract was evaporated down to a solid, and to this residue was added 180 ml. of hot water. The resulting solution was cooled to 2° and 4.5 g. of acidic material that melted at 275° was filtered off. The filtrate was evaporated down on a steam-bath to 8.41 g. of a light tan colored solid of m.p. 157–167°. A portion of this was recrystallized from acetone to yield *cis*-2,5-*p*-dioxanedicarboxylic acid of m.p. 178°. The yield was *ca.* 11%. One gram of this acid can be dissolved in less than 0.8 ml. of water at 0°. The mixed m.p. with *trans*-2,5-*p*-dioxanedicarboxylic acid is not depressed; melting began at 178° and continued to *ca.* 250°. The mixed melting point with *cis*-2,6-*p*-dioxanedicarboxylic acid[1] of melting point 177–178°, was 149–155°.

Anal. Calcd. for $C_6H_8O_6$: C, 40.91; H, 4.58; neut. equiv., 88. Found: C, 41.08; H, 4.66; neut. equiv., 88.

B. **V to IV.**—In a solution of 1.76 g. of potassium hydroxide and 6.23 ml. of water was dissolved 0.22 g. (0.00125 mole) of *cis*-2,5-*p*-dioxanedicarboxylic acid. This solution was heated on a steam-bath for 19 hours with intermittent addition of water to keep the concentration of potassium hydroxide at about 20%. The solution was then acidified with concd. hydrochloric acid. An additional 10 ml. of water was then added to the solution which was cooled in an ice-bath. The organic acid that precipitated was filtered off, washed twice with cold water, then dried at 50° to constant weight. The solid hydrate weighed 0.154 g. (64%). It was heated 15 minutes at 115°. It then weighed 0.142 g. (64%), and melted at 275°. The mixed melting point with authentic *trans*-2,5-*p*-dioxanedicarboxylic acid was undepressed.

C. **The Action of Concd. Hydrochloric or Nitric Acid on IV and V.**—Solutions containing 40 mg. of *cis*-2,5-*p*-dioxanedicarboxylic acid (V) dissolved in 2 ml. of the hot concentrated mineral acids were heated five hours at 100°. The solutions were then evaporated down to a volume of 0.5 ml. and cooled to 0°. No precipitates were evident. Upon complete evaporation of the solutions the residues melted sharply at 178° and were not depressed by admixture with the starting material. There was no evidence of any trace of the very insoluble *trans* isomer, IV. Similar experiments with IV as a starting material yielded no evidence of isomerization to V.

The Partial Resolution of *cis*-2,5-*p*-Dioxanedicarboxylic Acid.—To an acetone solution of 449 mg. (1.14 mmoles) of brucine was added 200 mg. (1.14 mmoles) of *cis* 2,5-*p*-dioxanedicarboxylic acid dissolved in acetone. An immediate white precipitate was obtained. Additional acetone was added until the precipitate was dissolved. The solution was then left standing four days. The first crop (264 mg.) of brucine salt was filtered off and to it was added one ml. of concd. ammonium hydroxide. To the mixture containing precipitated brucine was then added 2 ml. of chloroform with vigorous shaking. The resulting two liquid layers were separated and the ammoniacal layer was extracted twice with chloroform, filtered and put in a one-decimeter polarimeter tube. The solution was 1.02 ± 0.05° levorotatory.

Continued fractionation of the brucine salt produced a last crop, which when worked up as above produced an ammoniacal solution of the *cis*-2,5-*p*-dioxanedicarboxylic acid salt that was 0.20 ± 0.05° dextrorotatory.

Using the same procedure as above on the *trans*-2,5-*p*-dioxanedicarboxylic acid produced no material that rotated polarized light.

***trans*-Dimethyl 2,5-*p*-Dioxanedicarboxylate (VI).**—Nine and thirty-six hundredths grams (0.48 mole) of *trans*-2,5-*p*-dioxanedicarboxylic acid monohydrate was dissolved in 140 ml. of hot methanol. The solution was cooled to 15°, and anhydrous hydrogen chloride was passed through it with external cooling until the solution was saturated. The resulting mixture (white precipitate) was allowed to stand two days, then cooled to 0° and filtered. The mother liquor was concentrated to yield additional solid. The combined solids were washed with cold bicarbonate solution until carbon dioxide was no longer evolved. The solid was then washed with cold water until the wash was neutral. The wet solid was recrystallized from methanol yielding 7.34 g. (75%), of colorless crystals of m.p. 143°.

Anal. Calcd. for $C_8H_{12}O_6$: C, 47.06; H, 5.93. Found: C, 47.27; H, 5.98.

The same ester could be obtained by the action of an ethereal solution of diazomethane on the acid. But owing to the insolubility of the acid and its dimethyl ester in ethyl ether, the reaction is slow and the above procedure is recommended for the preparation of *trans*-dimethyl 2,5-*p*-dioxanedicarboxylate. The diazomethane synthesis is reported because this reagent would not alter the configuration.

***cis*-Dimethyl 2,5-*p*-Dioxanedicarboxylate (VII). A.**—This ester was prepared using the same procedure as for the preparation on *trans*-dimethyl 2,5-dioxanedicarboxylate from methanol and hydrogen chloride. However, the ester was soluble in the reaction mixture and did not precipitate until excess methanol and hydrogen chloride were removed by evaporation at reduced pressure. From 5 g. (0.028 mole) of the acid was obtained 2.77 g. (48%) of *cis*-dimethyl 2,5-*p*-dioxanedicarboxylate of m.p. 92°.

B. **From Diazomethane.**—Two hundred and sixty-two milligrams of *cis*-2,5-*p*-dioxanedicarboxylic acid was partially dissolved in 30 ml. of ethyl ether. To this suspension was added an ethereal solution of diazomethane until the yellow color persisted. The excess diazomethane and ether were evaporated off, and the crystalline residue of m.p. 91° was recrystallized from ligroin to a m.p. of 92°. This ester when mixed with that of the preceding preparation melted at 92°.

Anal. Calcd. for $C_8H_{12}O_6$: C, 47.06; H, 5.93. Found: C, 46.97; H, 5.64.

MIXED MELTING POINTS OF *cis*- AND *trans*-DIMETHYL 2,5-*p*-DIOXANEDICARBOXYLATES AND SOME OF THEIR 3,6-ISOMERS

Mixtures	M.p., °C.	Pure cmpds.	M.p., °C.
cis-2,5 and *trans*-2,5	85	*cis*-2,5	92
cis-2,5 and *cis*-2,6	70	*trans*-2,5	143
cis-2,5 and *trans*-2,6	67	*cis*-2,6	103
trans-2,5 and *trans*-2,6	83	*trans*-2,6	89
trans-2,5 and *cis*-2,6	95		
trans-2,6 and *cis*-2,6	70		

***trans*-2,5-*p*-Dioxanedicarboxylicdiacetic Anhydride (VIII).**—To 100 ml. of boiling acetic anhydride in an open vessel was slowly added 11.92 g. (0.0678 mole) of *trans*-2,5-*p*-dioxanedicarboxylic acid. All but a trace dissolved. The hot solution was filtered and cooled to 10°. A copious precipitate was obtained which was filtered and washed with benzene and pentane. It weighed 14.15 g. (80%) and melted at 135°. The m.p. could not be raised by recrystallization from benzene, but when the entire yield was recrystallized from 500 ml. of boiling acetic anhydride, the m.p. rose to 145°. The m.p. of a portion of this recrystallized again from a large volume of acetic anhydride was 151°. A further recrystallization from acetic anhydride did not raise the melting point. (The material on heating at atmospheric pressure melts at 151° then loses acetic anhydride and resolidifies at 160°.) If this material is heated to *ca.* 150° at 5 mm. of pressure it does not melt but sublimes unchanged. It dissolves in warm water which upon cooling precipitates *trans*-2,5-*p*-dioxanedicarboxylic acid of m.p. 275°.

Anal. Calcd. for $C_{10}H_{12}O_8$: C, 46.16; H, 4.65; neut. equiv., 65. Found: C, 46.40; H, 4.67; neut. equiv., 66.

Poly-*trans*-2,5-*p*-dioxanedicarboxylic Anhydride (IX).—*trans*-2,5-*p*-Dioxanedicarboxylicdiacetic anhydride was melted in a large test-tube open to the atmosphere. The tube was heated by means of an oil-bath slowly to a temperature of *ca.* 170° where acetic anhydride distilled off and the melt resolidified. The pressure on the tube was then reduced to 5 mm. and the temperature of the bath was kept at 170° for 15 minutes to remove all acetic anhydride. A white brittle solid remained which did not melt but discolored slowly over the temperature range 210–240°. The solid when hydrolyzed by warm dilute hydrochloric acid forms an acid of m.p. 275° which did not depress the melting point of authentic *trans*-2,5-*p*-dioxanedicarboxylic acid. The white brittle solid was presumably poly-*trans*-2,5-*p*-dioxanedicarboxylic anhydride.

2,5-*p*-Dioxanedicarboxylic Anhydride (X).—Three and twenty-seven hundredths grams of poly-*trans*-2,5-*p*-dioxanedicarboxylic anhydride was placed in a 500-ml. distilling flask. The side-arm of the flask led to a 25-ml. distilling flask which was used as the receiver and was cooled by an ice-bath. The pressure on the system was reduced to 5 mm. and the contents of the large flask were heated with an open flame. 2.36 g. (72% crude yield) of a yellow wax-like solid was obtained as the distillate. The addition of 25 ml. of benzene to the distillate dissolved most of it. The benzene solution was then filtered into 300 ml. of pentane. A white solid precipitated. The pentane solution was decanted and the solid was washed twice with pentane. It was then filtered and dried at room temperature and 5 mm. of pressure. The melting point of this freshly prepared monomeric 2,5-*p*-dioxanedicarboxylic anhydride was 75–77°. It is very sensitive to moisture in the atmosphere and in solvents. Upon standing in a desiccator the m.p. slowly rises, presumably due to polymerization. A molecular weight determination of the freshly prepared anhydride cryscopically in benzene was 168. The theoretical molecular weight for monomeric 2,5-*p*-dioxanedicarboxylic anhydride is 158. The anhydride dissolved readily in water, and upon evaporation to dryness of the aqueous solution, material of m.p. 178° was the only product. The mixed melting point of this hydrolysis product and that of the 2,5-*p*-dioxanedicarboxylic acid that could be partially resolved was 178°.

The Conversion of *cis*-Dimethyl 2,5-*p*-Dioxanedicarboxylate (VII) to *cis*-2,5-Bis-(iodomethyl)-*p*-dioxane (XIII). A. *cis*-2,5-Bis-(hydroxymethyl)-*p*-dioxane (XI).—A solution of 2.6 g. (0.013 mole) of *cis*-dimethyl 2,5-*p*-dioxanedicarboxylate in 200 ml. of ethyl ether was added in 45 minutes to a stirred slurry of 2 g. (0.052 mole) of lithium aluminum hydride in 150 ml. of ethyl ether. The reaction mixture was cooled externally and no refluxing took place during the addition. The mixture was refluxed 20 minutes. It was cooled and to it was slowly added 5 ml. of water dissolved in 15 ml. of methanol. The mixture was then left to decompose overnight. It was filtered through glass wool and the filtrate evaporated down to 20 ml. To this was added 200 ml. of benzene and the mixture was boiled to remove water, methanol and ether. The solution was filtered from inorganic material and evaporated down with heating under a stream of nitrogen to *ca.* 0.23 g. of a colorless oil which could not be crystallized.

B. *cis*-2,5-Bis-(*p*-toluenesulfonatomethyl)-*p*-dioxane (XII).—Following the method of Tipson[12] the *p*-toluenesulfonate derivative was made of the oil from the preceding experiment. The *cis*-2,5-bis-(*p*-toluenesulfonatomethyl)-*p*-dioxane weighed 0.70 g. (12% yield from the dimethyl ester) and melted at 85–87°. It was recrystallized from a benzene–ligroin mixture to a m.p. of 88°.

Anal. Calcd. for $C_{20}H_{24}O_8S_2$: C, 52.62; H, 5.30; S, 14.06. Found: C, 52.84; H, 5.42; S, 13.66.

C. *cis*-2,5-Bis-(iodomethyl)-*p*-dioxane (XIII).—To 428 mg. (0.94 mmole) of *cis*-2,5-bis-(*p*-toluenesulfonatomethyl)-*p*-dioxane and 2 g. (0.013 mole) of sodium iodide was added 20 ml. of dry acetone. The mixture was then refluxed 4.25 hours. The acetone solvent was evaporated off and to the residue was added 50 ml. of water. The water insoluble reaction product was filtered and dried. The product weighed 324 mg. (94%) and melted at 95°. After recrystallization from methanol it melted at 97°. When mixed with *trans*-2,5-bis-(iodomethyl)-*p*-dioxane it melted over the range 90–135°; the two iodides were only partially soluble.

Anal. Calcd. for $C_6H_{10}I_2O_2$: C, 19.53; H, 2.74; I, 69.0. Found: C, 20.03; H, 2.82; I, 69.5.

The Conversion of *trans*-2,5-*p*-Dioxanedicarboxylic Acid (IV) to *trans*-2,5-Bis-(iodomethyl)-*p*-dioxane (I). A. The Lithium Aluminum Hydride Reduction of *trans*-2,5-*p*-Dioxanedicarboxylic Acid.—Fifty-four hundredths gram (0.017 mole) of *trans*-2,5-*p*-dioxanedicarboxylic acid in a porous thimble was slowly extracted into a refluxing mixture of 2 g. (0.053 mole) of lithium aluminum hydride and 200 ml. of ethyl ether. The operation was carried out in a Soxhlet apparatus and required 19 hours of refluxing. A water–ethanol solution was then added slowly to the reaction mixture until the excess reagent was decomposed. The mixture was filtered, and the filtrate evaporated almost to dryness. To this residue benzene was added and the mixture was boiled until all water was removed azeotropically. On cooling, the filtered benzene solution precipitated 0.07 g. of crystals of m.p. 91°. The mother liquor on evaporation gave 0.17 g. of additional crystals of m.p. 90°. This product when mixed with authentic *trans*-2,5-bis-(hydroxymethyl)-*p*-dioxane melted at 91°. The yield was 0.24 g. (53%).

B. *trans*-2,5-Bis-(*p*-toluenesulfonatomethyl)-*p*-dioxane (XIV).—Following the method of Tipson[8] the *p*-toluenesulfonate derivative was made from 1 g. (0.0067 mole) of *trans*-2,5-bis-(hydroxymethyl)-*p*-dioxane. The crude dry product melted at 197–200° and weighed 1.94 g. (63%). It was recrystallized from a benzene–methanol solution and washed with hexane. It then melted at 205°.

Anal. Calcd. for $C_{20}H_{24}O_8S_2$: C, 52.62; H, 5.30. Found: C, 52.39; H, 5.23.

C. The Conversion of *trans*-2,5-Bis-(*p*-toluenesulfonatomethyl)-*p*-dioxane (XIV) to *trans*-2,5-Bis-(iodomethyl)-*p*-dioxane (I).—A solution of 1 g. (0.0022 mole) of *trans*-2,5-bis-(*p*-toluenesulfonatomethyl)-*p*-dioxane and 2.64 g. (0.0176 mole) of sodium iodide in 75 ml. of dry acetone was refluxed for 14 hours. The solvent was evaporated off and 50 ml. of water added to the residue. The resulting mixture was filtered and the insoluble reaction product was washed with water and dried. The product weighed 0.72 g. (89%) and melted at 148–150°. It was recrystallized from ethanol to a m.p. of 157°, and this mixed with authentic *trans*-2,5-bis-(iodomethyl)-*p*-dioxane (I) melted at 158°.

***trans*-2-Iodomethyl-5-acetoxymethyl-*p*-dioxane.**—A mixture of 20 g. (0.054 mole) of *trans*-2,5-bis-(iodomethyl)-*p*-dioxane, 12.3 g. (0.127 mole) of freshly fused and powdered potassium acetate and 35 ml. of glacial acetic acid was refluxed 17 hours, then cooled and added to 250 ml. of water. The insoluble matter was filtered off and the filtrate made weakly basic with concentrated sodium hydroxide. This precipitated additional solid. The combined dry precipitates were heated with 400 ml. of hexane, which was then cooled to room temperature and filtered. The undissolved matter was mainly unreacted starting material. The filtrate on evaporation yielded a solid that melted at *ca.* 60–70°. It was extracted by 600 ml. of hot water. On cooling the aqueous solution, 4.04 g. (24%) of crystals precipitated. They melted at 68°, and, by an element test, were found to contain iodine. Recrystallization from hexane did not raise the melting point.

Anal. Calcd. for $C_8H_{13}O_4I$: C, 31.70; H, 4.32. Found: C, 32.07; H, 4.54.

***trans*-2-Iodomethyl-5-*p*-dioxanecarboxylic Acid.**—This compound was detected in less than 1% yield by an attempted oxidation of *trans*-2,5-bis-(iodomethyl)-*p*-dioxane to *trans*-2,5-*p*-dioxanedicarboxylic acid using the procedure of Fischer[13] for the conversion of 2,5-bis-(hydroxymethyl)-3,6-bis-(benzyloxy)-*p*-dioxane to 3,6-bis-(benzyloxy)-2,5-*p*-dioxanedicarboxylic acid. The dioxane was recrystallized from toluene to yield crystals of m.p. 148°, that contained iodine.

Anal. Calcd. for $C_6H_9O_4I$: C, 26.49; H, 3.33. Found: C, 26.87; H, 3.35.

***trans*-2-Iodomethyl-5-phenylaminomethyl-*p*-dioxane and *trans*-2,5-Bis-(phenylaminomethyl)-*p*-dioxane.**—A solution of 5 g. (0.014 mole) of *trans*-2,5-bis-(iodomethyl)-*p*-dioxane, 12.7 g. (0.14 mole) of aniline and 50 ml. of b.p. 140° "xylene" was refluxed eight hours. The reaction mixture was added to 100 ml. of 10% hydrochloric acid; and this mixture was then steam distilled until only unreacted starting material and water distilled over. The residue was cooled and filtered from additional starting material. The aqueous acidic solution was made basic with 15 g. of solid sodium hydroxide and steam distilled until excess aniline was removed. The solid amine residue did not distil. It was filtered off and extracted with 40 ml. of boiling hexane.

The hexane extract was evaporated down to a brown-

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(12) R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

(13) H. O. L. Fischer, E. Baer and H. Nidecker, *Helv. Chim. Acta*, **20**, 1227 (1937).

colored oil which, when recrystallized from methanol, yielded 0.30 g. of a solid that melted at 70°. The solid was recrystallized again from an ethanol–water solution containing a trace of sodium hydroxide to a m.p. of 72°. It was shown to contain iodine and nitrogen by an element test. The yield was *ca.* 7%.

Anal. Calcd. for $C_{12}H_{16}NO_2I$: C, 43.26; H, 4.84; N, 4.20. Found: C, 43.80; H, 4.93; N, 4.34.

The solid unextracted by hexane was dissolved in hot benzene. The benzene solution was evaporated down to a solid that weighed 0.69 g. and melted at 160–165°. It was recrystallized from a mixture of ethanol and benzene containing a trace of sodium hydroxide to crystals of m.p. 166–169°. The results of an element test showed that they contained nitrogen but no iodine. The yield was 15%.

Anal. Calcd. for $C_{13}H_{22}N_2O_2$: C, 72.45; H, 7.43; N, 9.39. Found: C, 72.58; H, 7.41; N, 9.45.

***trans*-2,5-Bis-(aminomethyl)-*p*-dioxane (XVI).**—Two grams (0.0054 mole) of *trans*-2,5-bis-(iodomethyl)-*p*-dioxane and 30 ml. of concd. ammonium hydroxide were heated in a sealed tube for three hours at 140°. The solution obtained was boiled to expel excess ammonia and to reduce the volume. Solid sodium hydroxide was then added and the dark-colored solid that precipitated out was filtered and extracted by hot ethanol. The ethanol solution was evaporated down to a solid that was sublimed under 11 mm. of pressure. The sublimate consisted of 0.50 g. (63%) of colorless crystals of m.p. 134°.

Anal. Calcd. for $C_6H_{14}N_2O_2$: N, 19.17. Found: N, 18.83.

Usual procedures were used to convert this amine to a dibenzamide XVIII, m.p. 235°, identical in most properties to that reported by Stoehr, although his melting point was 229°. On one occasion we used a sample of diamine unpurified by sublimation and duplicated Stoehr's melting point.[6]

Anal. Calcd. for $C_{20}H_{22}O_4N_2$: N, 7.91. Found: N, 7.93.

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EVANSTON, ILLINOIS

NOTES

The Benzoylation of Dibenzofuran

BY ROBERT G. JOHNSON, H. B. WILLIS AND HENRY GILMAN

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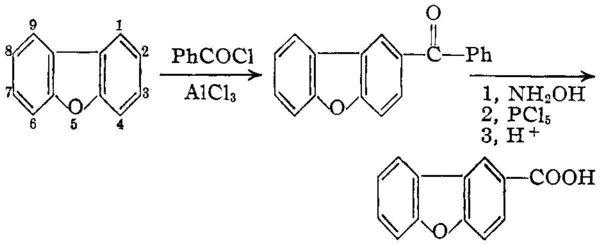
The benzoyldibenzofuran obtained as a result of the action of benzoyl chloride on dibenzofuran has been reported[1] as having the melting point 167–168°.

We have found that the Friedel–Crafts reaction of dibenzofuran with an excess of benzoyl chloride yields two ketones, one melting at 136–138°, the other at 167–168.5°.

Analysis of the two ketones and their oximes indicated that the compound melting at 136–138° is a monobenzoyldibenzofuran, while the higher melting ketone (apparently the compound obtained by Borsche and Bothe) is a dibenzoyldibenzofuran.

The structure of the monoketone has been established as 2-benzoyldibenzofuran by virtue of the fact that this compound was also obtained when (1) benzonitrile was treated with 2-dibenzofuryllithium and (2) phenyllithium was allowed to react with 2-dibenzofurancarboxylic acid diethylamide. Further proof of the structure was afforded by conversion of the ketoxime to an amide *via* the Beckman rearrangement, the amide yielding 2-dibenzofurancarboxylic acid on acid hydrolysis.



It is assumed that the diketone is 2,8-dibenzoyldibenzofuran.[2] Though the dioxime was prepared, it could not be rearranged to the diamide. Several attempts to do so yielded in each instance material which melted over a wide range and which could not be purified by recrystallization.

2-Benzamidodibenzofuran and 2,8-dibenzamidodibenzofuran, the products to be expected from the Beckmann rearrangement of the *syn*-phenyl oximes,[3] have been prepared.

Experimental[4]

Benzoylation of Dibenzofuran.—The Friedel–Crafts reaction of 43.7 g. (0.26 mole) of dibenzofuran with 59.0 g. (48.7 ml., 0.42 mole) of benzoyl chloride and 53.0 g. of aluminum chloride in 400 ml. of nitrobenzene was carried out at room temperature for 14 hours. Subsequent to hydrolysis, the nitrobenzene was removed by steam distillation. The residue after washing with a 5% solution of sodium hydroxide and then with methanol weighed 76.8 g. and melted over the range 110–128°. Recrystallization from ethanol–benzene and then from glacial acetic acid (three times) gave a product which melted over the range 130–136°, softening at 115°. Chromatography from benzene solution on an alumina column and recrystallization from glacial acetic acid of all fractions melting above 130° gave 28.2 g. (39.8%) of white needles, m.p. 134–137.5°. A sample of **2-benzoyldibenzofuran** purified for analysis by recrystallization from glacial acetic acid melted at 136–138°.

Anal. Calcd. for $C_{19}H_{12}O_2$: C, 83.80; H, 4.44. Found: C, 83.72, 83.72; H, 4.50, 4.56.

The mother liquors from the ethanol–benzene recrystallization of the monobenzoyl compound were worked up to give 2.94 g. (3.0%) of **2,8-dibenzoyldibenzofuran**, m.p. 167–168.5°, after two recrystallizations from glacial acetic acid.

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[1] W. Borsche and W. Bothe, *Ber.*, **41**, 1940 (1908).

[2] Both diacetylation [H. Gilman, P. T. Parker, J. C. Bailie and G. E. Brown, THIS JOURNAL, **61**, 2836 (1939)] and dipropionylation [Ng. Ph. Buu-Hoi and R. Royer, *Rec. trav. chim.*, **67**, 175 (1948)] give 2,8-disubstituted dibenzofurans.

[3] The *anti*-phenyl configuration has been assigned by us to the 2-benzoyldibenzofuran oxime reported in this note because of the generalization [B. Jones, *Chem. Revs.*, **35**, 335 (1944)] that *trans* migration occurs in the Beckmann rearrangement.

[4] All melting points are uncorrected.