

twenty-four hours at room temperature a 3.0-ml. sample was titrated for formic acid and residual oxidant. On a molar basis 1.93 moles of oxidant was consumed while 0.95 mole of formic acid was formed.

**2,3,4-Tribenzoyl-D-ribose.**—To a solution of 1.0 g. of 2,3,4-tribenzoyl- $\beta$ -D-ribofuranosyl bromide in 10 ml. of acetone was added 1 ml. of water and 1 g. of silver carbonate. The suspension was shaken at room temperature for two hours, filtered, treated with carbon and refiltered. Concentration *in vacuo* gave a sirup which rotated  $-27.9^\circ$  in chloroform (*c*, 1.130).

**Methyl 2,3,4-Tribenzoyl- $\beta$ -D-ribofuranoside from 2,3,4-Tribenzoyl-D-ribose.**—A solution of 0.73 g. of sirupy 2,3,4-tribenzoyl-D-ribose in 10 ml. of methyl iodide was shaken at  $2^\circ$  with 1 g. of silver oxide for six days. After filtration, the methyl iodide was removed *in vacuo*, leaving a residue of 0.765 g. of sirup which rotated  $-54.8^\circ$  in chloroform (*c*, 1.114). After solution of the sirup in 2 ml. of methanol and seeding with authentic methyl 2,3,4-tribenzoyl- $\beta$ -D-ribofuranoside it gave 0.605 g. (80%) of crystalline material whose melting point, either alone or when mixed with authentic methyl 2,3,4-tribenzoyl- $\beta$ -D-ribofuranoside, was  $108-109^\circ$ .

### Summary

Reaction of 2,3,4-tribenzoyl- $\beta$ -D-ribofuranosyl

bromide with methanol alone gives satisfactory yields of methyl 2,3,4-tribenzoyl- $\beta$ -D-ribose, identical with the tribenzoate from the previously known methyl  $\beta$ -D-ribofuranoside.

Ethanol similarly converts 2,3,4-tribenzoyl- $\beta$ -D-ribofuranosyl bromide into ethyl 2,3,4-tribenzoyl- $\beta$ -D-ribofuranoside which on catalytic debenzoylation yielded ethyl  $\beta$ -D-ribofuranoside, identical with the product made directly by the interaction of D-ribose with ethanolic hydrogen chloride.

Reaction of 2,3,4-tribenzoyl- $\beta$ -D-ribofuranosyl bromide with aqueous acetone has given amorphous 2,3,4-tribenzoyl-D-ribose whose structure was confirmed through methylation to methyl 2,3,4-tribenzoyl- $\beta$ -D-ribofuranoside.

The advantage in the use of 2,3,4-tribenzoyl- $\beta$ -D-ribofuranosyl bromide for the preparation of ribofuranosides has been pointed out.

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## Unsymmetrical Analogs of DDT<sup>1</sup>

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A considerable number of ring-substituted derivatives of 1-trichloro-2-diphenylethane—so-called analogs of DDT—have been described. However, in the special case of analogs in which each of the two phenyl groups bears a different substituent, the compounds to be found in the literature are fewer in number.<sup>4</sup>

The unsymmetrical analogs have been prepared in which the substituent on one phenyl group is a chlorine atom and that on the other phenyl group is a bromine or an iodine atom. In addition, the first two members of a series of analogs have been prepared in which the substituent on one phenyl group is a methoxy group and that on the other phenyl group is a hydroxy or higher alkoxy group. Attempts to prepare the unsymmetrical analog having a para chlorine atom on one benzene ring and a para methoxy group on the other were unsuccessful.

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(4) Fleck and Haller, *THIS JOURNAL*, **66**, 2095 (1944); Cristol, *ibid.*, **67**, 1494 (1945); Anonymous, *Chem. Eng. News*, **23**, 1520 (1945); Prill, *et al.*, *Contribs. Boyce Thompson Inst.*, **14**, 341 (1946); Haller, *et al.*, *THIS JOURNAL*, **67**, 1591 (1945); Lauger, *et al.*, "Mechanism of Intoxication of DDT Insecticides in Insects and Warm-blooded Animals," Geigy Co., New York, 1946; Chattaway and Muir, *J. Chem. Soc.*, 701 (1934).

In the preparation of these analogs, the 1-trichloro-2-(substituted phenyl)-ethanols were employed as intermediates.

Dinesmann<sup>5</sup> in 1905 prepared 1-trichloro-2-phenylethanol and its *p*-methoxy derivative in 80% yield by the condensation of benzene or anisole with chloral in the presence of anhydrous aluminum chloride. von Leuthold<sup>6</sup> applied this method to the preparation of the *p*-chlorophenyl compound. On the other hand, Frankforter and Kritchevsky<sup>7,8</sup> working with aluminum chloride as the condensing agent for alkyl and alkoxy derivatives of benzene obtained not the respective carbinols, but instead 1-trichlorodiphenylethanes in good yields. These workers were unable to reconcile their results with those of Dinesmann. They postulated two distinct reaction mechanisms, namely, that of the Grignard and the Friedel-Crafts (Dinesmann) reactions, in which simple condensation takes place and no water is eliminated, and secondly that obtaining in the Baeyer sulfuric acid condensation and their own reaction using aluminum chloride, where a molecule of water is eliminated with the formation of a 1-trichloro-2-diphenylethane.

Chattaway and Muir<sup>4</sup> showed that the carbinols were intermediates in the Baeyer condensation of

(5) Dinesmann, *Compt. rend.*, **141**, 201 (1905).

(6) von Leuthold, French Patent 791,172 (Dec. 5, 1935); *Chem. Abstr.*, **30**, 3157 (1936).

(7) Frankforter and Kritchevsky, original communication to the 8th Int. Congr. of Applied Chem., (Appendix), **25**, 361 (1912).

(8) Frankforter and Kritchevsky, *THIS JOURNAL*, **36**, 1511 (1914); **37**, 385 (1915).

chloral with benzene derivatives to give 1-trichloro-2-diarylethanes. By reversing the customary order of mixing the reagents, and adding the benzene derivative to an excess of chloral mixed with acid, they obtained a considerable quantity of the carbinol. The latter readily underwent condensation with a second molecule of the benzene derivative to form a 1-trichlorodiarylethane.

Therefore, the Baeyer condensation takes place not in one step as formulated by Frankforter, but actually in two steps, namely, an aldol condensation which yields a 1-trichloromethyl-2-arylethanol, followed by a reaction between the carbinol and a second molecule of the benzene derivative, yielding a 1-trichloro-2-diarylethane with the loss of a molecule of water. Haller and his co-workers identified in technical DDT the carbinol itself and several related compounds whose occurrence they explained on the basis of such a mechanism.

The experimental results herein described indicate that the aluminum chloride condensation, like the Baeyer sulfuric acid condensation, proceeds by way of an intermediate 1-trichloro-2-arylethanol. Unlike the Baeyer reaction, the aluminum chloride reaction under a given set of conditions, may undergo both phases, or merely the first, depending upon the nature of the substituent on the benzene ring. In the condensation of chloral with chlorobenzene under the conditions of Dinesmann, a good yield of 1-trichloro-2-*p*-chlorophenylethanol was obtained along with only a small quantity of DDT. On the other hand, with anisole the reaction proceeded through the second step and a 90% yield of 1-trichloro-2,2-bis-(*p*-methoxyphenyl)-ethane was obtained. Under the same conditions, 1-trichloro-2-*p*-methoxyphenylethanol prepared by another method condensed readily with anisole, with phenetole, and with phenol to form the respective DDT analogs. However, the methoxyphenylethanol could not be made to condense with chlorobenzene in the presence of aluminum chloride to form 1-trichloro-2-*p*-chlorophenyl-2-*p*-methoxyphenylethane. Nor could the latter be prepared under these conditions from 1-trichloro-2-*p*-chlorophenylethanol and anisole. Neither of these reactions could be carried out by means of sulfuric acid, because in each case the *p*-chloro component was resistant to condensation under conditions mild enough to avoid the sulfonation of the methoxy component. Other condensing agents were also tried without success. This compound would be interesting as a possible insecticidal agent, since it would be a hybrid between DDT and its insecticidally effective methoxy analog, known as methoxychlor.<sup>9</sup>

The use of aluminum chloride as the condensing agent under the conditions of Dinesmann for the preparation of methoxychlor (1-trichloro-2,2-bis-(*p*-methoxyphenyl)-ethane) from chloral and ani-

sole has been found practical. It offers advantage over the Baeyer reaction as a commercial procedure, for in the absence of significant side reactions such as condensation in the *o*,*p'*-positions, a product of high purity is obtained in good yield, and equipment and operational costs are low because of the low viscosity of the reaction mixture, the ability to operate at room temperature, and the small quantity of heat evolved in the reaction.

### Experimental

**1-Trichloro-2-*p*-chlorophenyl-2-*p*-bromophenylethane, (I).**—To a vigorously stirred mixture of 36.6 g. of bromobenzene and 66 ml. of 100% sulfuric acid was added dropwise 31.2 g. of 1-trichloro-2-*p*-chlorophenylethanol (II). The temperature was kept at 60°. The addition consumed one hour, and before it was complete a crystalline product had appeared in the reaction mixture. The stirring was maintained for an additional period of three hours. The reaction mass was poured onto shaved ice and the solid product which separated was collected by filtration and washed in turn with several portions of water, with a saturated solution of sodium bicarbonate, and finally with a small quantity of ethanol. The product after one crystallization from a mixture of chloroform and ethanol weighed 29.2 g., representing a yield 61.0% of the theoretical. After further purification by crystallization from the same solvent, 20.8 g. was obtained of a product melting at 124.3–124.5° (cor.).

*Anal.* Calcd.: C, 42.15; H, 2.27; Cl, 35.55; Br, 20.03. Found: C, 42.41; H, 2.61; Cl, 35.01; Br, 21.54.

**1-Dichloro-2-*p*-chlorophenyl-2-*p*-bromophenylethane.**—Ten grams of I was heated under reflux in ethanol solution with 5 g. of potassium hydroxide for one and one-half hours. Upon dilution with water and cooling, 9 g. of crystals was obtained, m. p. 105–106° (uncor.) representing a yield of 98.6% of the theoretical. Recrystallization from ethanol gave a product melting at 105.8–106.5° (cor.).

*Anal.* Calcd.: C, 46.38; H, 2.22; AgX (mg. per mg. sample), 1.704. Found: C, 46.07, H, 2.27, AgX (mg. per mg. sample), 1.689.

A solution of 2 g. of the olefin in 10 g. of glacial acetic acid was heated under reflux while 1 g. of chromium trioxide was added in small portions. The heating was continued during one hour and then the solution was cooled and poured onto ice. The solid material which separated was crystallized from a mixture of chloroform and ethanol; the yield was 0.78 g. of lustrous scales (60.0% of the theoretical). After several recrystallizations the product melted at 148.5–149.0° (cor.). The m. p. was not lowered by the admixture of *p*,*p'*-bromochlorobenzophenone prepared by the method of Gomberg.<sup>10</sup>

*Anal.* Calcd.: C, 52.82; H, 2.73; AgX (mg. per mg. sample), 1.120. Found: C, 53.07; H, 3.60; AgX (mg. per mg. sample), 1.108.

**1-Trichloro-2-*p*-chlorophenyl-2-*p*-iodophenylethane (III).**—Following the procedure described in the case of the chloro-bromo analog, 47 g. of iodobenzene was treated with 30.9 g. of II in the presence of 78 ml. of 100% sulfuric acid. The yield of crystallized product was 29.6 g. (55.8% of the theoretical). The product after recrystallization from a mixture of chloroform and ethanol melted at 126.5–127.0° (cor.).

*Anal.* Calcd.: C, 37.70; H, 2.03; AgX (mg. per mg. sample), 1.812. Found: C, 37.91; H, 2.72; AgX, 1.794.

**1-Dichloro-2-*p*-chlorophenyl-2-*p*-iodophenylethane** was obtained by heating 5 g. of III with a solution of potassium hydroxide in ethanol. After several recrystallizations from ethanol the ethylene weighed 4.3 g. (93.6% of the theoretical yield) and melted at 112–112.3° (cor.).

(9) Anon., *Chem. Eng. News*, **26**, 476 (1948).

(10) Gomberg and Bailar, *This Journal*, **51**, 2229 (1929).

*Anal.* Calcd.: C, 41.06; H, 1.97; AgX (mg. per mg. sample), 1.646. Found: C, 42.07; H, 2.68; AgX (mg. per mg. sample), 1.593.

The ethylene was oxidized to 4-chloro-4'-iodobenzophenone by treating 2 g. dissolved in boiling glacial acetic acid with 1 g. of chromium trioxide. The yield after crystallization from a mixture of chloroform and ethanol was 1.3 g. (77.7% of the theoretical) of a product melting at 157–163.5° (cor.). After several recrystallizations from the same solvent, the melting point was 171.2–171.7° (cor.). This ketone, as well as the parent chloro-iodo analog and the corresponding ethylene, is a new compound, and the assignment of the para position to the iodine atom is justified by analogy to the chloro-bromo analog and also to DDT itself.

*Anal.* Calcd.: C, 45.57; H, 2.35; AgX (mg. per mg. sample), 1.130. Found: C, 45.82; H, 2.75; AgX (mg. per mg. sample), 1.128.

**1-Trichloro-2-*p*-methoxyphenyl-2-*p*-ethoxyphenylethane.**—To a mixture of 1 g. of 1-trichloro-2-*p*-methoxyphenylethanol (IV) and 3.5 g. of phenetole was added 0.2 g. of anhydrous aluminum chloride<sup>11</sup> in one portion and the mixture was shaken vigorously. The aluminum chloride dissolved in the mixture of the reactants and the solution rapidly acquired a deep violet color and its viscosity gradually increased. The mixture was shaken three times at hourly intervals, and then was allowed to stand overnight. Then it was poured into water and the oil which separated was washed with water, steam distilled, and extracted with chloroform. Upon evaporation of the chloroform, a viscous oil remained which crystallized on standing. Upon recrystallization from dilute ethanol, 1 g. (71.0% of the theoretical yield) of crystals was obtained, melting at 86–87°. Since this melting point was close to that of the methoxy analog itself, namely, 88–89°, a mixed melting point was determined, and was found to be 75–77°. After another crystallization, the methoxy-ethoxy analog melted at 86.2–87.0° (cor.).

*Anal.* Calcd.: C, 56.76; H, 4.76; Cl, 29.57. Found: C, 57.14; H, 5.50; Cl, 29.07.

**1-Trichloro-2-*p*-methoxyphenyl-2-hydroxyphenylethane.**—When a mixture of 1 g. of IV and 2.15 g. of anhydrous phenol was treated with 0.2 g. of aluminum chloride as in the preceding paragraph, a yield of 1.1 g. was obtained of a material melting at 113–115° (uncor.) which was believed to be the methoxy-hydroxy analog (82.7% of the theoretical yield). It was not further characterized.

**1-Trichloro-2-*p*-chlorophenyl-2-*p*-methoxyphenylethane.**—This compound was not obtained when II was treated with anisole, or IV with chlorobenzene, in the presence of aluminum chloride according to the procedure outlined above. In each case the carbinol was recovered essentially unchanged from the diluted reaction mixture after removal of the steam-volatile component. When concentrated sulfuric acid was used as the condensing agent, the methoxy-containing component—whether anisole or the carbinol—underwent sulfonation and the desired reaction did not proceed. In an attempt to avoid sulfonation, acetic acid was used as a diluent as follows:

To a well-stirred solution of 16.5 g. of anisole in a mixture of 42 ml. each of concentrated sulfuric acid and glacial acetic acid was added 20 g. of II over a period of one hour. The mixture was stirred for six hours and allowed to stand fifteen hours. The acetate of the carbinol was obtained in a yield of 20.9 g. (89.9% of theoretical). After two crys-

tallizations from ethanol its melting point of 125.0–125.5° (cor.) agreed with the previously published value.<sup>12</sup>

*Anal.* Calcd.: C, 39.77; H, 2.67; Cl, 46.96; mol. wt., 302.0; sapon. equiv., 60.40. Found: C, 40.07; H, 3.04; Cl, 46.64; mol. wt. (Rast), 322; sapon. equiv., 60.03.

Five equivalents of alkali are consumed in the saponification: one in the hydrolysis of the ester and four in the hydrolysis of the alkyl chlorine atoms and the neutralization of the resulting acid. The liberated chloride ion was determined and the results were in good agreement with the alkalimetric results.

The formation of the acetate of the carbinol under these conditions resembles Cristol's obtaining an almost quantitative yield of the diacetate of bromal hydrate in an attempt to condense bromal with chlorobenzene by means of sulfuric acid, using acetic acid as the solvent.<sup>13</sup>

The desired reaction also failed to take place in the presence of chlorosulfonic acid by the procedure of Rueggeberg.<sup>14</sup>

**1-Trichloro-2,2-bis-(*p*-methoxyphenyl)-ethane (Methoxychlor).**—A mixture of 747 g. of freshly distilled anisole and 150 g. of anhydrous chloral was treated under vigorous stirring with 33 g. of freshly powdered anhydrous aluminum chloride, added in small portions, over a period of one hour. The vigorous stirring was maintained during a total of twelve hours, and then the solution was allowed to stand for ten hours. It was then poured into cold water and the oil which separated was washed with diluted hydrochloric acid and with water. The unreacted anisole was recovered by steam distillation. After the steam distillation of the unreacted anisole, a very viscous liquid remained, a small quantity of which crystallized immediately when rubbed with a few drops of ethanol. It was, therefore, crystallized from a mixture of chloroform and ethanol, yielding 313.5 g. of a product melting at 88 to 89°, as compared with 89° for pure methoxychlor. This yield was 89.1% of the theoretical. The melting point indicated that the product was substantially entirely the desired para substituted product. The melting point was not lowered by the admixture of methoxychlor prepared by the sulfuric acid condensation.<sup>15</sup>

### Summary

1. A group of unsymmetrical *p,p'*-analogs of DDT have been prepared.
2. In the case of hydroxy and alkoxy analogs, a new, convenient method of preparation has been described in which aluminum chloride is used as the condensing agent.
3. The latter procedure is suitable for the commercial production of the *p,p'* dimethoxy analog of DDT.
4. Evidence has been presented that the aluminum chloride condensation of benzene derivatives with chloral to yield DDT analogs proceeds by a mechanism analogous to the Baeyer condensation.

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(12) Howard and Castles, *THIS JOURNAL*, **57**, 376 (1935).

(13) Cristol and Haller, *ibid.*, **66**, 140 (1946).

(14) Rueggeberg and Torrains, *Ind. Eng. Chem.*, **38**, 211 (1946).

(15) Fritsch and Feldman, *Ann.*, **306**, 77 (1899).

(11) Eastman Kodak Co.