

## INVESTIGATIONS IN THE DDT SERIES

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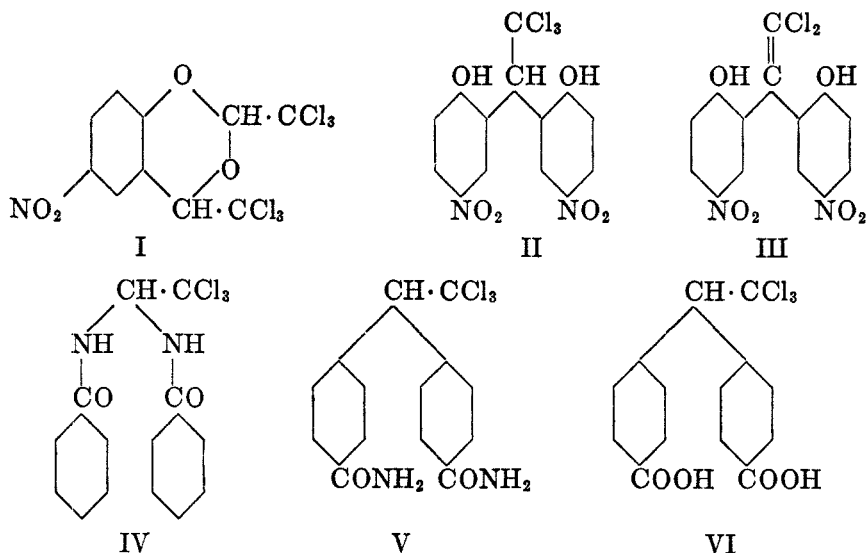
In a previous paper (1) the condensation of fluorene with chloral was described, but the position in which the condensation took place had not been elucidated. We have now found that dehydrohalogenation of the 1,1-difluorenyl-2,2,2-trichloroethane and subsequent oxidation with chromic acid leads to a difluorenyl ketone which has the melting point (297–298°) given in the literature (2) for the 2,2'-compound. In accordance with the well-known rules for the substitution in the fluorene nucleus (3), the condensation with chloral appears to take place in the 2- position.

In our previous publication, the reaction of chloral with 2-nitrophenol has been described. We have reinvestigated the condensation of chloral with the *p*-isomer under the influence of fuming sulfuric acid. Chattaway (4) has isolated substance (I) from this reaction, in which 1 mole of the phenol has condensed with 2 moles of chloral. We have found that under the conditions employed in our experiments the yield of (I) is only 2.5%, whilst a yield of 15% was obtained of a second substance melting at 179° which, in contradistinction to (I), is soluble in alkali. It is undoubtedly the expected substance of formula (II), as indicated by the fact that methanolic alkali splits off 1 mole of hydrochloric acid, giving in 61% yield a substance of m.p. 225–226° which according to the analyses is the corresponding ethylene (III).

We have extended our investigation to the condensation of chloral hydrate with benzonitrile. Under the influence of sulfuric acid a yield of 60%, under the influence of chlorosulfonic acid a yield of 85%, was obtained of a substance melting at 271° and corresponding to the formula  $C_{10}H_{13}Cl_3N_2O_2$ . To this substance Hepp and Spiess (5) have ascribed formula (IV), whilst Martin and Wain (6) assumed (with some reservation) that normal condensation has taken place, accompanied by hydrolysis of the cyano to amide groups (V). The hydrolysis of the substance with either sulfuric acid in glacial acetic acid or with aqueous alkali gives benzoic acid, however, and equally the treatment with methanolic sodium hydroxide gives benzamide. Formula (IV) appears, therefore, to represent the structure of the substance. In order to verify this conclusion, we have prepared the amide (V) by an unambiguous method: by condensation of toluene with chloral, according to Fischer (7), we have obtained in 53% yield the 1,1-di(*p*-tolyl)-2,2,2-trichloroethane, which was oxidized by means of sodium dichromate and concentrated sulfuric acid to the corresponding dicarboxylic acid (VI), m.p. 271–272°. This was converted *via* the dichloride into the diamide of m.p. 227°. This substance which had definitely formula (V), was not identical with the condensation product of benzonitrile and chloral hydrate.

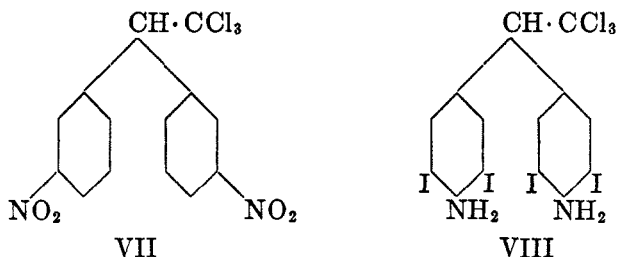
As benzamide does not react with chloral under the conditions employed for

benzocnitrile, one has to conclude that the observed hydrolysis of the cyano group does not take place before the condensation, but follows it.



In our previous communication it was shown that 1,1-diphenyl-2,2,2-trichloroethane is nitrated mainly in the two *p*-positions. Investigation of the mother liquors has led to the isolation of a second isomer of m.p. 118°. This contains the nitro groups in the *m*-positions to the side chain (VII): dehydrohalogenation led to a 1,1-dinitrophenyl-2,2-dichloroethylene of m.p. 128–129° which could be oxidized to 3,3'-dinitrobenzophenone of m.p. 160°, identical with that described by Staedel (8).

In view of the interest which the previously described 1,1-di-(4'-amino-phenyl)-2,2,2-trichloroethane exhibits as tuberculostatic agent, several derivatives were prepared. Treatment with iodine monochloride in glacial acetic acid gave a tetraiodo derivative of m.p. 145° (dec.) which by analogy (9) should be ascribed the following formula (10) (VIII).

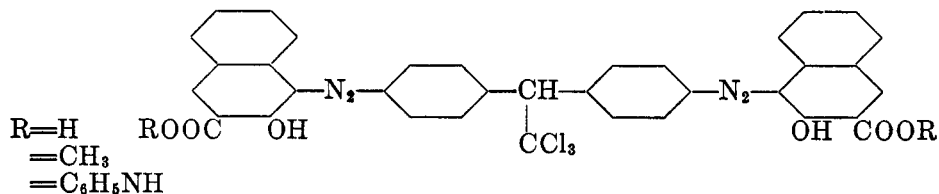


Also the bis(trichloroacetyl) derivative of m.p. 199° was prepared in which the lipophilic character should be enhanced in comparison with the parent substance (11). It forms a molecular compound with 1 mole of benzene

Furthermore, we have used the diamino compound for the preparation of some

azo dyes. After diazotization of both amino groups, it was coupled with 2-hydroxynaphthalene-3-carboxylic acid, its methyl ester, and its anilide, respectively. All three dye-stuffs (IX) were obtained in pure form, while those with  $\alpha$ - and  $\beta$ -naphthylamine could not be purified completely.

Attention is drawn to the fact that in the meantime the same diamino compound has been described by Balaban and Levy (12).<sup>1</sup>



### EXPERIMENTAL

*Di-(2-fluorenyl) ketone.* Just 0.5 g. of the previously described 1,1-difluorenyl-2,2-dichloroethylene was oxidized with 1.5 g. of chromic acid in 10 cc. of glacial acetic acid at the boiling temperature. The green reaction mixture was diluted with water and the solid product which separated was recrystallized from glacial acetic acid. The lemon-yellow crystals melted at 297–298° as indicated by Dziejowsky and Panek (2) and gave the correct analytical figures.

*Anal.* Calc'd for  $C_{27}H_{14}O_2$ : C, 83.9; H, 3.6.

Found: C, 83.9; H, 4.2.

*Condensation of chloral hydrate and p-nitrophenol.* To a mixture of 20 g. of *p*-nitrophenol, 15 g. of concentrated and 15 g. of fuming sulfuric acid, 11 g. of chloral hydrate, diluted with 10 g. of concentrated and 10 g. of fuming sulfuric acid, was added slowly with vigorous stirring. The stirring was continued for 8 hours without cooling and the product was poured onto crushed ice. It was then filtered, washed with warm water and triturated at 50° with 100 cc. of an aqueous 10% sodium hydroxide solution.

The filtrate was decolorized with active carbon and acidified with dilute hydrochloric acid. Four and three-tenths g. of 1,1-(2'-hydroxy-5'-nitrophenyl)-2,2,2-trichloroethane (II) separated and were recrystallized from toluene and glacial acetic acid; colorless prisms of m.p. 179°, yield, 15%.

*Anal.* Calc'd for  $C_{14}H_9Cl_3N_2O_6$ : C, 41.2; H, 2.2; N, 6.8.

Found: C, 41.5; H, 2.8; N, 6.4.

From dilute alcohol or dilute acetic acid, the substance crystallizes with 1 mole of water. The hydrate melts with gas evolution at 146°, solidifies again, and melts finally at 179°.

*Anal.* Calc'd for  $C_{14}H_9Cl_3N_2O_6 \cdot H_2O$ :  $H_2O$ , 4.2. Found:  $H_2O$ , 4.6.

The alkali-insoluble part (1.5 g.) was recrystallized from glacial acetic acid or alcohol; it melted at 144–145°. It was identical with the heterocyclic compound (I) described by Chattaway (4).

*Anal.* Calc'd for  $C_{10}H_5Cl_2NO_4$ : C, 28.8; H, 1.2.

Found: C, 29.1; H, 1.4.

1,1-(2'-Hydroxy-5'-nitrophenyl)-2,2-dichloroethylene. (III) The preceding substance

<sup>1</sup> In our previous communication (1), the assumption had been made that the product of m.p. 239–246° (dec.) described by BURGER, GRAF, AND BAILEY [*J. Am. Chem. Soc.*, **68**, 1725 (1946)] was the diacetyl derivative of the above di-*p*-amino compound which we had obtained. Dr. Burger has kindly informed us that this has been confirmed by determination of the mixed m.p. of the two respective samples.

(2 g.) was refluxed for 12 hours with a solution of 0.8 g. of sodium hydroxide in 10 cc. of methanol. A red precipitate was formed which was isolated by filtration, dissolved in water and acidified with dilute hydrochloric acid. Recrystallized from 60% alcohol or 50% acetic acid, m.p. 225-226°, yield, 61%.

*Anal.* Calc'd for  $C_{14}H_9Cl_2N_2O_4$ : C, 45.3; H, 2.1; N, 7.5.

Found: C, 45.1; H, 2.5; N, 7.9.

*Condensation of chloral hydrate with benzonitrile.* (a) To a cold mixture of 16 g. of chloral hydrate, 25 g. of concentrated and 25 g. of fuming sulfuric acid, 20 g. of benzonitrile was added with vigorous stirring. The addition caused only a slight rise in temperature. After one hour, the mixture was diluted with ice and the product filtered, washed and recrystallized from glacial acetic acid; long, soft needles of m.p. 271° (dec.), yield 60%.

(b) To a solution of 3.2 g. of chloral hydrate in 15 cc. of carbon tetrachloride, was added with stirring at 20°, 2.3 g. of chlorosulfonic acid. After 10 minutes, 4.1 g. of benzonitrile was added, followed by another 2.5 g. of chlorosulfonic acid. The exothermic reaction was checked by external cooling, and the product, after an hour, treated as above, yield 85%. The analysis and the following hydrolysis experiments show that the substance is the *N,N*-dibenzoyl derivative of 1,1-diamino-2,2,2-trichloroethane (IV).

*Anal.* Calc'd for  $C_{18}H_{13}Cl_2N_2O_7$ : C, 51.6; H, 3.5; N, 7.5.

Found: C, 51.6; H, 3.5; N, 7.7.

*Hydrolysis.* (a) A mixture of 2 g. of IV, 2 cc. of 50% sulfuric acid and 3 cc. of glacial acetic acid was refluxed for 3 hours. The reaction product was precipitated by addition of water and identified as *benzoic acid*.

(b) A mixture of 1 g. of IV and 10 cc. of a 10% aqueous sodium hydroxide solution was refluxed for 5 hours. The product was pure *benzoic acid*.

(c) A mixture of 3.7 g. of IV, 0.5 g. of sodium hydroxide and 50 cc. of methyl alcohol was refluxed for 5 hours. The solvent was removed and the residue dried on a porous plate and recrystallized from butyl alcohol. The crystals (1 g.) melted at 128° and were identified as *benzamide*.

*Condensation of chloral hydrate with toluene.* According to Fischer (7), 600 g. of concentrated sulfuric acid was added, at ice temperature and with violent agitation, to a mixture of 165 g. of chloral hydrate and 202 g. of toluene. The stirring was continued for 3 hours, and the viscous mass poured onto crushed ice. The crude product was washed with water and triturated with 200 cc. of alcohol. From 1200 cc. of alcohol, white platelets of 1,1-di-(*p*-tolyl)-2,2,2-trichloroethane, m.p. 89°, yield, 53%.

*1,1-Di-(p-carboxyphenyl)-2,2,2-trichloroethane (VI).* To a mixture of 76.6 g. of potassium dichromate, 26.6 g. of the preceding substance, and 150 cc. of water, was added, with stirring, 170 g. of concentrated sulfuric acid. When half of this quantity was added, the mixture began to warm up; it was heated to the boiling point, and the addition was continued at the boiling temperature. A viscous product precipitated. The reaction mixture was diluted with 1 liter of water, and the solid material ground, washed with 300 cc. of 5% sulfuric acid and water, and extracted with 200 cc. of 5% aqueous sodium hydroxide solution. The desired dicarboxylic acid was precipitated by means of dilute sulfuric acid and recrystallized from 50% alcohol or nitrobenzene; needles of m.p. 271-272° (dec.), yield 20%.

*Anal.* Calc'd for  $C_{16}H_{11}Cl_2O_4$ : C, 51.5; H, 2.9; Neut. equiv., 373.

Found: C, 52.0; H, 3.1; Neut. equiv., 374.

*1,1-Di-(p-carboxamidophenyl)-2,2,2-trichloroethane (V).* A mixture of 4 g. of the dicarboxylic acid and 12 cc. of thionyl chloride was refluxed for 3 hours. The excess chloride was removed by distillation and the remaining viscous yellow oil taken up in ether and added slowly to a concentrated aqueous ammonia solution. The yellowish precipitate was washed with water and recrystallized from methanol or glacial acetic acid; transparent platelets of m.p. 227° (dec.), yield, quantitative.

*Anal.* Calc'd for  $C_{16}H_{13}Cl_2N_2O_2$ : C, 51.7; H, 3.5; N, 7.5.

Found: C, 52.0; H, 3.7; N, 7.4.

*1,1-Di-(3'-nitrophenyl)-2,2,2-trichloroethane.* From the glacial acetic acid mother

liquors of the di-*para*- nitro compound, colorless crystals separated upon standing. They were recrystallized several times from the same solvent and formed well-shaped prisms of m.p. 118°.

*Anal.* Calc'd for  $C_{14}H_9Cl_2N_2O_4$ : C, 44.9; H, 2.4.

Found: C, 44.3; H, 2.6.

*1,1-Di-(3'-nitrophenyl)-2,2-dichloroethylene.* A mixture of 1.8 g. of the preceding substance with a solution of 0.5 g. of potassium hydroxide in 25 cc. of methanol was boiled under reflux for 4 hours. The reaction product crystallized upon cooling, and was filtered, washed with water, dried, and recrystallized from butanol; m.p. 128–129°, yield 82.3%.

*Anal.* Calc'd for  $C_{14}H_9Cl_2N_2O_4$ : C, 49.2; H, 2.3.

Found: C, 49.8; H, 2.0.

*Oxidation.* To a boiling solution of 0.5 g. of the nitroethylene in 5 cc. of glacial acetic acid, 1 g. of chromic acid in 5 cc. of the same solvent was slowly added, and the boiling was continued for 4 hours. The reaction product was poured onto crushed ice; the oil which separated, solidified spontaneously; from glacial acetic acid, plates which showed the correct m.p. 160° of 3,3'-dinitrobenzophenone.

*1,1-Di-(3',5'-diiodo-4'-aminophenyl)-2,2,2-trichloroethane.* To a solution of 1 g. of the diamino compound in 5 cc. of glacial acetic acid, was added gradually a solution of 2.5 g. of iodine monochloride in 5 cc. of the same solvent. The reaction was accompanied by a rise in temperature. After 12 hours, the mixture was diluted with water, filtered, and the solid material washed with sodium bisulfite solution; from methyl alcohol, m.p. 145° (dec.).

*Anal.* Calc'd for  $C_{14}H_9Cl_3I_2N_2$ : C, 20.5; H, 1.2; N, 3.4.

Found: C, 20.7; H, 1.4; N, 3.8.

*1,1-Di-(4'-trichloroacetylaminophenyl)-2,2,2-trichloroethane.* To an ice-cold solution of 3.2 g. of the diamino compound, 2 g. of pyridine, and 40 cc. of chloroform, was added, drop by drop, 3.6 g. of trichloroacetyl chloride. After 12 hours, the clear reaction mixture was treated with water, and the solvent evaporated to dryness. The residue was triturated with petroleum ether and recrystallized from a mixture of the same solvent with butyl alcohol; m.p. 198.5°, yield 58%.

*Anal.* Calc'd for  $C_{18}H_{11}Cl_5N_2O_2$ : C, 35.6; H, 1.8; N, 4.6.

Found: C, 36.2; H, 1.7, N, 4.5.

From benzene, the product crystallizes with 1 mole of the solvent. This solvate melts at 142° with gas evolution, solidifies again, and melts finally at 198°.

*Anal.* Calc'd for  $C_{18}H_{11}Cl_5N_2O_2 \cdot C_6H_6$ : C, 42.1; H, 2.4; N, 4.1.

Found: C, 42.4; H, 4.2; N, 4.6.

*Dye-stuff from 1,1-di-(4'-aminophenyl)-2,2,2-trichloroethane and 2-hydroxy-3-naphthoic acid.* A solution of 3.15 g. of the diamino compound in a mixture of 6 cc. of concentrated hydrochloric acid and 20 cc. of water was diazotized at 0° with a solution of 1.4 g. of sodium nitrite in 4 cc. of water. By addition of 0.5 g. of sodium carbonate, the solution was neutralized and it was dropped at ice temperature into a solution of 3.6 g. of 2-hydroxy-3-naphthoic acid and 2.12 g. of sodium carbonate in 40 cc. of water. By filtration and thorough washing with water, there was obtained 7.5 g. of the dye-stuff in the form of a red powder, which crystallized slowly from a mixture of xylene or isoamyl alcohol with nitrobenzene, and melted then at 207° (with decomposition).

*Anal.* Calc'd for  $C_{38}H_{23}Cl_3N_4O_6$ : C, 60.6; H, 3.2; N, 9.1.

Found: C, 60.7; H, 3.6; N, 9.1.

*Dye-stuff from 1,1-di-(4'-aminophenyl)-2,2,2-trichloroethane and 2-hydroxy-3-naphthanilide.* The diazonium salt, prepared and neutralized as in the previous example, was coupled at 0° with 50 cc. of an aqueous solution of 5.3 g. of 2-hydroxy-3-naphthanilide, containing 3 cc. of 30% sodium hydroxide solution. The reaction product was treated with dilute hydrochloric acid and the solid recrystallized from nitrobenzene diluted with some butanol; clusters of red crystals which melt at 235–240° (dec.).

*Anal.* Calc'd for  $C_{48}H_{33}Cl_3N_6O_4$ : C, 66.7; H, 3.8; N, 9.7.

Found: C, 67.4; H, 4.3; N, 10.0.

*Dye-stuff from 1,1-di-(4'-aminophenyl)-2,2,2-trichloroethane and methyl 2-hydroxy-3-naphthoate.* The diazonium solution, prepared as in the preceding examples, was added to a solution of 4.2 g. of methyl 2-hydroxy-3-naphthoate in 30 cc. of water containing 3 cc. of 30% sodium hydroxide solution. A red product precipitated. The reaction mixture was acidified and the product washed with water; recrystallized from nitrobenzene, m.p. 185-190° (dec.).

*Anal.* Calc'd for  $C_{37}H_{27}Cl_3N_4O_6$ : C, 64.3; H, 3.8.

Found: C, 63.9; H, 3.8.

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