CCCLXIV.—*The Interaction of Chloral and* 2 : 4 : 6-*Trihalogen-substituted Phenylhydrazines.*

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IT has recently been shown (Chattaway and Bennett, J., 1927, 2850) that the violence of the reaction which occurs when chloral and phenylhydrazine are brought together is so moderated by the presence of halogen atoms in the hydrazine nucleus that the products, which differ according to the solvent in which the reaction takes place, can be isolated.

The reaction between chloral and the 2 : 4 : 6-trihalogen-substituted phenylhydrazines proceeds with such smoothness that its course can be completely followed. When chloral reacts with 2 : 4 : 6-trichlorophenylhydrazine, for example, it at first behaves normally, yielding a pale yellow hydrazone (I); this compound is extremely unstable and loses hydrogen chloride rapidly at the ordinary temperature, giving a compound (II) of a brilliant crimson colour which is indifferent to acetic anhydride and yields 2 : 4 : 6-trichloroaniline on reduction : it must therefore have an azo-structure and its composition shows it to be *αα-dichloro-β-*2 : 4 : 6-*trichlorobenzeneazoethylene.*

The elimination of hydrogen chloride from the initially formed hydrazone is a reversible reaction, for when a solution of the azo-compound (II) in hot acetic anhydride is saturated with hydrogen chloride, *chloral-α-acetyl-*2 : 4 : 6-*trichlorophenylhydrazone* is formed. The reaction may therefore be expressed :

$$\mathrm{NHX{\cdot}NH_2 + CCl_3{\cdot}CHO \longrightarrow \underset{(I.)}{[NHX{\cdot}N{:}CH{\cdot}CCl_3]} \rightleftarrows \underset{(II.)}{NX{:}N{\cdot}CH{:}CCl_2} + HCl.}$$

$$[\mathrm{X = C_6H_2Cl_3(2:4:6)}].$$

Further evidence confirming the constitution of the crimson condensation product is afforded by the action of halogens upon it.

It combines with chlorine, for example, to give a yellow addition product (III), which from its colour must be regarded as having a hydrazone structure, the hydrogen atom previously attached to the methine carbon atom now being attached to the α-nitrogen atom. This compound, like the structurally analogous hydrazone (I), loses hydrogen chloride on warming with acetic acid or acetic anhydride, the colour reverting to crimson, since the azo-structure is re-established, the methine chlorine-substituted azo-compound, ααβ - *trichloro* - β - 2 : 4 : 6 - *trichlorobenzeneazoethylene* (IV), being formed.

$$\text{(III.)}\ \mathrm{NHX{\cdot}N{:}CCl{\cdot}CCl_3 \longrightarrow NX{:}N{\cdot}CCl{:}CCl_2 + HCl}\ \text{(IV.)}$$

When the crimson compound (II) is heated with acetic acid containing hydrogen chloride, it is converted into *glyoxylic acid* 2 : 4 : 6-*trichlorophenylhydrazone*, and if it is heated with alcoholic hydrogen chloride, *ethyl glyoxylate* 2 : 4 : 6-*trichlorophenylhydrazone* is formed, the action in each case depending on the reversible nature of the elimination of hydrogen chloride from the 2 : 4 : 6-trichlorophenylhydrazone of chloral. This behaviour explains the formation of an alkyl glyoxylate 2 : 4 : 6-trichlorophenylhydrazone when chloral reacts with 2 : 4 : 6-trichlorophenylhydrazine in the corresponding alcohol.

The formation of the 2 : 4 : 6-trichlorophenylhydrazones of glyoxylic acid or the alkyl glyoxylates is due to the hydrolysis of the CCl_3 group of the chloralphenylhydrazone, but this is a much slower reaction than the elimination of hydrogen chloride; consequently, when the reaction between chloral and 2 : 4 : 6-trichlorophenylhydrazine takes place in acetic acid or alcoholic solution, there first occurs an almost complete formation of the azo-ethylene, which, as the hydrolysis proceeds, again combines with the hydrogen chloride.

When the reaction takes place in alcoholic solution, the reaction mixture turns brilliant crimson and the azo-ethylene can be isolated from it, but the colour gradually disappears as recombination with hydrogen chloride takes place and hydrolysis proceeds.

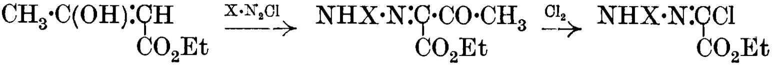
The formation of the glyoxylic acid and alkyl glyoxylate phenylhydrazones is therefore much facilitated by the presence of excess of hydrogen chloride during the reaction, which may be represented

$$\mathrm{NX{:}N{\cdot}CH{:}CCl_2 + HCl \rightleftharpoons NHX{\cdot}N{:}CH{\cdot}CCl_3 \xrightarrow{ROH} NHX{\cdot}N{:}CH{\cdot}CO_2R.}$$

The action of halogens upon the 2 : 4 : 6-trichlorophenylhydrazones of glyoxylic acid or its esters yields the corresponding ω-halogenated hydrazones, which are also formed when the azo-compounds (IV) are heated in presence of hydrogen chloride with acetic acid or alcohol, respectively.

$$NHX\cdot N{:}CH\cdot CO_2R \xrightarrow{Cl_2} NHX\cdot N{:}CCl\cdot CO_2R \xleftarrow[HCl]{ROH} NX{:}N\cdot CCl{:}CCl_2.$$

ω-Halogenated alkyl glyoxylate 2 : 4 : 6-trichlorophenylhydrazones can also be obtained by esterification of the corresponding ω-halogenated glyoxylic acid 2 : 4 : 6-trichlorophenylhydrazones, and very readily by the action of chlorine or bromine on *ethyl* 2 : 4 : 6-*trichlorobenzeneazoacetoacetate,* prepared by coupling 2 : 4 : 6-trichlorobenzenediazonium chloride with ethyl acetoacetate (compare Bülow and Neber, *Ber.*, 1912, **45**, 3732); the acetyl group is removed and replaced by halogen; *e.g.*,



$$CH_3\cdot C(OH){:}\underset{CO_2Et}{CH} \xrightarrow{X\cdot N_2Cl} NHX\cdot N{:}\underset{CO_2Et}{C}\cdot CO\cdot CH_3 \xrightarrow{Cl_2} NHX\cdot N{:}\underset{CO_2Et}{CCl}$$

The stability of the ω-halogenated 2 : 4 : 6-trichlorophenylhydrazones of glyoxylic acid and its esters is remarkable : for instance, the halogen atom is not affected by boiling for a short time with alcoholic ammonia, a process which readily yields a hydrazidine in the case of the ω-halogenated benzaldehyde- and *m*-nitrobenzaldehyde-2 : 4 : 6-trichlorophenylhydrazones.

EXPERIMENTAL.

When condensation of chloral and an arylhydrazine takes place in aqueous solution, the azo-ethylene, being practically insoluble in this solvent, separates and comparatively little hydrolysis occurs; but with acetic acid or alcohol as solvent, the azo-ethylene is first formed, giving the reaction mixture an intense crimson colour, and unless the hydrogen chloride is removed, hydrolysis occurs, the crimson colour disappears, and the hydrazone of glyoxylic acid or its ester is formed. If, however, the acetic acid contains excess of sodium acetate, recombination with hydrogen chloride and hydrolysis are prevented, and the azo-ethylene can be isolated.

Action of 2 : 4 : 6-*Trichlorophenylhydrazine Hydrochloride on Chloral Hydrate.*—(1) *In aqueous solution.* Chloral hydrate (9 g.; 1 mol.) and 2 : 4 : 6-trichlorophenylhydrazine hydrochloride (13·5 g.; 1 mol.) were dissolved in 1000 c.c. of hot water containing 20 c.c. of hydrochloric acid, and the mixture was heated nearly to boiling. As the temperature approached 80°, the liquid became turbid and *αα-dichloro-*β-2 : 4 : 6-*trichlorobenzeneazoethylene* separated in minute drops which coalesced to a viscid liquid of a brilliant crimson colour and solidified on cooling to a hard crimson cake. It crystallised from alcohol, in which it was very easily soluble, in deep crimson, acicular plates, m. p. 54° (Found : Cl, 58·05. $C_8H_3N_2Cl_5$ requires Cl, 58·25%).

(2) *In acetic acid solution in presence of sodium acetate.* The same quantities of reactants in 40 c.c. of acetic acid were warmed to 60°, the liquid turning deep crimson and hydrogen chloride being evolved; 8 g. (2 mols.) of finely powdered, anhydrous sodium acetate were then added, the mixture was heated on a water-bath for ½ hour, and the αα-dichloro-β-2 : 4 : 6-trichlorobenzeneazoethylene, which separated as a dark red liquid and solidified on cooling, was crystallised from alcohol.

(3) *In acetic acid solution.* If in the foregoing experiment, the mixture was heated to boiling without the addition of sodium acetate, after 10 minutes the colour had faded to orange, and on cooling, glyoxylic acid 2 : 4 : 6-trichlorophenylhydrazone separated. It crystallised from acetic acid, in which it was extremely soluble, in pale yellow, elongated plates, m. p. 167° (decomp.), identical with specimens prepared by direct synthesis.

(4) *In ethyl-alcoholic solution.* The hydrazine hydrochloride (12 g.; 1 mol.) was suspended in 50 c.c. of ethyl alcohol and 8 g. (1 mol.) of chloral hydrate were added; on being warmed for a few minutes, the solution turned crimson owing to the formation of the αα-dichloro-β-2 : 4 : 6-trichlorobenzeneazoethylene, for when a portion of the clear liquid was cooled, that compound separated. On further heating, the crimson colour slowly faded, and after an hour's boiling a clear yellow solution was obtained from which *ethyl glyoxylate* 2 : 4 : 6-*trichlorophenylhydrazone* separated on cooling. When crystallised from boiling alcohol, in which it was very soluble, it separated in pale yellow prisms, the colour deepening on exposure to daylight; m. p. 97·5° (Found : Cl, 36·1. $C_{10}H_9O_2N_2Cl_3$ requires Cl, 36·0%).

Reactions of αα-*Dichloro*-β-2 : 4 : 6-*trichlorobenzeneazoethylene.*—(1) *With alcohol.* 5 G. of the foregoing benzeneazoethylene were boiled with 25 c.c. of alcohol : after 8 hours, the crimson colour had changed to pale yellow, and on cooling, ethyl glyoxylate 2 : 4 : 6-trichlorophenylhydrazone separated. In a similar experiment in which the alcohol was first saturated with hydrogen chloride, the reaction was complete after 1 hour's boiling.

(2) *Formation of chloral*-α-*acetyl*-2 : 4 : 6-*trichlorophenylhydrazone.* A solution of 5 g. of αα-dichloro-β-2 : 4 : 6-trichlorobenzeneazoethylene in 10 c.c. of acetic anhydride was saturated at 80° with dry hydrogen chloride; the crimson colour faded rapidly, and on cooling, *chloral*-α-*acetyl*-2 : 4 : 6-*trichlorophenylhydrazone* separated as a colourless solid. It crystallised from boiling alcohol, in which it was readily soluble, in colourless rhombs, m. p. 144° (Found : N, 7·4; Cl, 55·25. $C_{10}H_8ON_2Cl_6$ requires N, 7·3; Cl, 55·5%).

(3) *Action of chlorine.* A stream of chlorine was passed into a well-cooled suspension of 10 g. of αα-dichloro-β-2 : 4 : 6-trichlorobenzeneazoethylene in 10 c.c. of acetic acid; the temperature rose slightly, and the solid dissolved, giving a pale orange solution from which *chloral-ω-chloro-*2 : 4 : 6*-trichlorophenylhydrazone* separated as a red, oily liquid; this solidified on standing with the mother-liquor, and crystallised from boiling acetone, in which it was easily soluble, in small yellow prisms, m. p. 104° (Found: N, 7·2; Cl, 66·0. $C_8H_3N_2Cl_7$ requires N, 7·5; Cl, 66·2%).

If the pale orange solution was heated to boiling, hydrogen chloride was evolved and the crimson colour restored; on cooling, *ααβ-trichloro*-β-2 : 4 : 6*-trichlorobenzeneazoethylene* was deposited. It crystallised from alcohol, in which it was readily soluble, in long, bright red needles, m. p. 75° (Found : Cl, 63·0. $C_8H_2N_2Cl_6$ requires Cl, 62·8%).

(4) *Action of bromine.* 2 C.c. (1 mol. + excess) of bromine dissolved in 5 c.c. of acetic acid were added to 5 g. (1 mol.) of αα-dichloro-β-2 : 4 : 6-trichlorobenzeneazoethylene suspended in 15 c.c. of acetic acid; the mixture was heated at 60° for 20 minutes and then cooled; the *αα-dichloro-α-bromo-*β-2 : 4 : 6*-trichlorobenzeneazoethylene* which separated crystallised from alcohol, in which it was easily soluble, in brick-red needles, m. p. 108·5° (Found : Cl, 46·1; Br, 20·7. $C_8H_2N_2Cl_5Br$ requires Cl, 46·2; Br, 20·75%).

Synthesis of Glyoxylic Acid and Ethyl Glyoxylate 2 : 4 : 6*-Trichlorophenylhydrazones.*—60 C.c. of 0·8*N*-glyoxylic acid solution (prepared by electro-reduction of oxalic acid) were added to 12 g. of 2 : 4 : 6-trichlorophenylhydrazine hydrochloride dissolved in 1000 c.c. of boiling water; *glyoxylic acid* 2 : 4 : 6*-trichlorophenylhydrazone* separated as a pale yellow, flocculent precipitate. It crystallised from hot acetic acid in pale yellow, elongated plates, m. p. 167° (decomp.) (Found : Cl, 39·7. $C_8H_5O_2N_2Cl_3$ requires Cl, 39·8%). When 5 g. of this compound were boiled for 6 hours with 25 c.c. of alcohol containing 2% of hydrogen chloride, and cooled, ethyl glyoxylate 2 : 4 : 6-trichlorophenylhydrazone separated as yellow prisms, m. p. 97·5°.

*Ethyl Glyoxylate α-Acetyl-*2 : 4 : 6*-trichlorophenylhydrazone.*—5 G. of ethyl glyoxylate 2 : 4 : 6-trichlorophenylhydrazone were dissolved in 10 c.c. of hot acetic anhydride and a drop of sulphuric acid was added; a violent reaction then set in. When the mixture was cooled, *ethyl glyoxylate α-acetyl-*2 : 4 : 6*-trichlorophenylhydrazone* separated. It crystallised from boiling alcohol, in which it was readily soluble, in colourless rhombs, m. p. 112·5° (Found : Cl, 31·6. $C_{12}H_{11}O_3N_2Cl_3$ requires Cl, 31·5%).

Action of Chlorine on Ethyl Glyoxylate 2 : 4 : 6*-Trichlorophenyl-*

hydrazone.—A stream of chlorine was passed into a suspension of 7 g. of ethyl glyoxylate 2 : 4 : 6-trichlorophenylhydrazone in 20 c.c. of acetic acid; the solid gradually dissolved and when a clear solution was obtained the whole was poured into water. *Ethyl glyoxylate* ω-*chloro*-2 : 4 : 6-*trichlorophenylhydrazone* immediately separated as a bulky, white solid; it crystallised from alcohol, in which it was easily soluble, in colourless plates, m. p. 73·5°, which turned pink on exposure to light (Found: Cl, 42·8. $C_{10}H_8O_2N_2Cl_4$ requires Cl, 43·0%).

This compound was also prepared by boiling a solution of 5 g. of ααβ-trichloro-β-2 : 4 : 6-trichlorobenzeneazoethylene in 25 c.c. of alcohol for 8 hours; the crimson colour slowly faded to pale yellow, and on cooling, the required compound separated. In a similar experiment, the alcohol was first saturated with hydrogen chloride and the reaction was then completed in an hour.

Action of Bromine on Ethyl Glyoxylate 2 : 4 : 6-*Trichlorophenylhydrazone.*—2 C.c. (1 mol. + excess) of bromine were added to 5 g. (1 mol.) of the hydrazone dissolved in 25 c.c. of acetic acid, and the mixture was heated at 60° for ½ hour; on cooling, *ethyl glyoxylate* ω-*bromo*-2 : 4 : 6-*trichlorophenylhydrazone* separated. It crystallised from alcohol, in which it was extremely soluble, separating in feathery, white plates, m. p. 75° (Found: Cl, 28·6; Br, 21·5. $C_{10}H_8O_2N_2Cl_3Br$ requires Cl, 28·4; Br, 21·3%).

Action of Chlorine on Glyoxylic Acid 2 : 4 : 6-*Trichlorophenylhydrazone.*—A stream of chlorine was passed into a suspension of 10 g. of glyoxylic acid 2 : 4 : 6-trichlorophenylhydrazone in 30 c.c. of acetic acid; the temperature rose and the solid all dissolved, and on cooling, *glyoxylic acid* ω-*chloro*-2 : 4 : 6-*trichlorophenylhydrazone* separated. It crystallised from hot acetic acid in small yellow prisms, m. p. 151·5° (decomp.) (Found: Cl, 47·1. $C_8H_4O_2N_2Cl_4$ requires Cl, 47·0%).

5 G. of the foregoing compound were esterified by boiling for 6 hours with 25 c.c. of alcohol containing 2% of hydrogen chloride; when the resulting yellow solution was cooled, ethyl glyoxylate ω-chloro-2 : 4 : 6-trichlorophenylhydrazone separated as white plates, m. p. 73·5°, identical with the compound described above.

Ethyl 2 : 4 : 6-*Trichlorobenzeneazoacetoacetate.*—20 G. (1 mol.) of 2 : 4 : 6-trichloroaniline were diazotised and the filtered solution was added slowly and with vigorous stirring to a well-cooled mixture of 13 g. (1 mol.) of ethyl acetoacetate dissolved in 200 c.c. of alcohol and 300 g. of sodium acetate in 1500 c.c. of water. The *ethyl* 2 : 4 : 6-*trichlorobenzeneazoacetoacetate* that separated crystallised from alcohol in small yellow prisms, m. p. 94·5° (Found: Cl, 31·4. $C_{12}H_{11}O_3N_2Cl_3$ requires Cl, 31·5%).

Action of Chlorine and of Bromine on Ethyl 2 : 4 : 6-*Trichlorobenzeneazoacetoacetate*.—When chlorine was passed into a suspension of 5 g. of the ester in 20 c.c. of acetic acid, heat was evolved; the pale yellow solution obtained, on cooling, deposited ethyl glyoxylate ω-chloro-2 : 4 : 6-trichlorophenylhydrazone as colourless plates, m. p. 73·5°, identical with specimens previously prepared.

2 C.c. of bromine (1 mol. + excess) in 5 c.c. of acetic acid were added to 5 g. (1 mol.) of ethyl 2 : 4 : 6-trichlorobenzeneazoacetoacetate in 20 c.c. of acetic acid and the mixture was heated at 60° for $\frac{1}{2}$ hour: on cooling, ethyl glyoxylate ω-bromo-2 : 4 : 6-trichlorophenylhydrazone separated in colourless needles, m. p. 75°, identical with the compound described above.

A similar series of reactions has been carried out with 2 : 4 : 6-tribromophenylhydrazine, and the following compounds prepared :— *αα-Dichloro-β-*2 : 4 : 6-*tribromobenzeneazoethylene*, crimson plates from alcohol, m. p. 92° (Found: C, 22·2; H, 0·9; N, 6·6; Cl, 16·2; Br, 54·7. $C_8H_3N_2Cl_2Br_3$ requires C, 21·9; H, 0·7; N, 6·4; Cl, 16·2; Br, 54·8%). *ααβ-Trichloro-β-*2 : 4 : 6-*tribromobenzeneazoethylene*, long, deep red, flat prisms from alcohol, m. p. 105° (Found: Cl, 22·4; Br, 50·6. $C_8H_2N_2Cl_3Br_3$ requires Cl, 22·5; Br, 50·8%). *αα-Dichloro-β-bromo-β-*2 : 4 : 6-*tribromobenzeneazoethylene*, flat, deep red prisms from alcohol, m. p. 115° (Found: Cl, 13·7; Br, 61·6. $C_8H_2N_2Cl_2Br_4$ requires Cl, 13·7; Br, 61·9%). *Glyoxylic acid* 2 : 4 : 6-*tribromophenylhydrazone*, faintly yellow, irregular plates from acetic acid, m. p. 170·5° (decomp.) (Found: Br, 59·6. $C_8H_5O_2N_2Br_3$ requires Br, 59·8%). *Ethyl glyoxylate* 2 : 4 : 6-*tribromophenylhydrazone*, pale yellow, flat prisms from alcohol, m. p. 126° (Found: C, 28·2; H, 2·1; N, 6·5; Br, 55·9. $C_{10}H_9O_2N_2Br_3$ requires C, 28·0; H, 2·1; N, 6·5; Br, 55·9%). *Ethyl glyoxylate α-acetyl-*2 : 4 : 6-*tribromophenylhydrazone*, colourless rhombs from alcohol, m. p. 133·5° (Found: C, 31·0; H, 2·4; N, 6·3; Br, 50·8. $C_{12}H_{11}O_3N_2Br_3$ requires C, 30·6; H, 2·4; N, 6·0; Br, 50·9%). *Ethyl glyoxylate ω-chloro-*2 : 4 : 6-*tribromophenylhydrazone*, colourless plates from alcohol, m. p. 108·5° (Found: Cl, 7·7; Br, 51·8. $C_{10}H_8O_2N_2ClBr_3$ requires Cl, 7·7; Br, 51·8%). *Ethyl glyoxylate ω-bromo-*2 : 4 : 6-*tribromophenylhydrazone*, elongated colourless plates from acetic acid, m. p. 102·5° (Found: Br, 62·8. $C_{10}H_8O_2N_2Br_4$ requires Br, 63·0%). *Ethyl* 2 : 4 : 6-*tribromobenzeneazoacetoacetate*, small yellow prisms from alcohol, m. p. 96·5° (Found: Br, 50·8. $C_{12}H_{11}O_3N_2Br_3$ requires Br, 50·9%).

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