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269. *The Action of Chlorine upon the Nitrophenylazoacetoacetates.*

By F. D. CHATTAWAY and D. R. ASHWORTH.

THE action of chlorine upon the nitrophenylazoacetoacetates differs considerably from the action of bromine upon these compounds, the position of the nitro-group in the phenyl residue having a more marked effect on the course of the reaction. This appears further to be profoundly conditioned by the nature of the solvent employed.

Thus when dry chlorine acts upon ethyl *p*-nitrophenylazoacetoacetate in dry chloroform, the acetyl group is replaced by chlorine with the formation of *ethyl α-chloroglyoxylate-*p*-nitrophenylhydrazone* (I). When, however, chlorination is effected in acetic acid in the presence of sodium acetate, both the acetyl group and the imino-hydrogen atom are replaced by chlorine, yielding *ethyl α-chloroglyoxylate-*N*-chloro-*p*-nitrophenylhydrazone* (II).

This is a comparatively stable compound, and can be heated with alcohol without change. When treated with hydriodic acid in acetic acid solution, the chlorine atom attached to nitrogen is replaced by hydrogen, yielding ethyl α-chloroglyoxylate-*p*-nitrophenylhydrazone identical with (I) above.

Indication of the formation of *N*-chloro-compounds, similar to the above, was also obtained when *ethyl 2-chloro-4-nitro-*, and *ethyl 2 : 6-dichloro-4-nitro-phenylazoacetoacetates*, dissolved in acetic acid in the presence of sodium acetate, were acted upon by chlorine,

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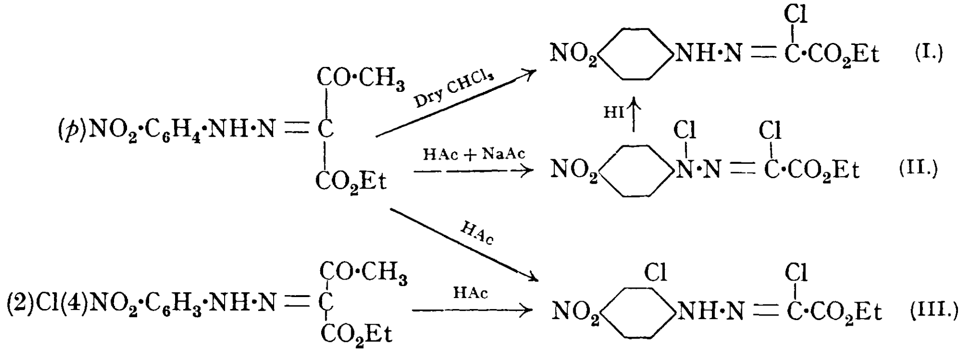
oily liquids being obtained which, on treatment with hydriodic acid, gave the corresponding α-chloroglyoxylatehydrazones.

When chlorination of ethyl *p*-nitrophenylazoacetoacetate is effected in acetic acid in the absence of sodium acetate, chlorine replaces the acetyl group, and enters the phenyl nucleus in an ortho-position, but does not replace the imino-hydrogen atom. The *ethyl α-chloroglyoxylate-2-chloro-4-nitrophenylhydrazone* (III) so formed is also obtained by the action of chlorine upon ethyl 2-chloro-4-nitrophenylazoacetoacetate in acetic acid solution.

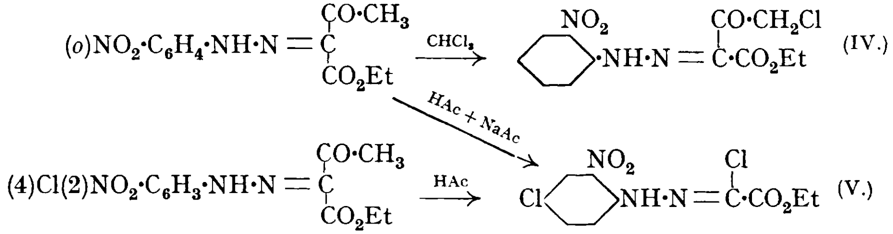


Under no conditions could the action of chlorine upon ethyl *p*-nitrophenylazoacetoacetate be so regulated as to effect substitution in the acetyl group, although the *p*-nitrophenylazo-γ-chloroacetoacetates anticipated were readily obtained by coupling the *p*-nitrophenyldiazonium salts with ethyl γ-chloroacetoacetate under normal conditions :

$$R{\cdot}N_2Cl + CH_2(CO{\cdot}CH_2Cl){\cdot}CO_2Et \longrightarrow R{\cdot}NH{\cdot}N{:}C(CO{\cdot}CH_2Cl){\cdot}CO_2Et$$

It is therefore specially noteworthy that the action of chlorine upon ethyl *o*-nitrophenylazoacetoacetate in chloroform solution gives a quantitative yield of *ethyl o-nitrophenylazo-γ-chloroacetoacetate* (IV), chlorine substituting, and not replacing, the acetyl group, and not entering the phenyl nucleus under these conditions.

Substitution in the *p*-position in the phenyl nucleus, and replacement of the acetyl group as a whole, however, takes place when *o*-nitrophenylazoacetoacetate dissolved in acetic acid, in the presence of sodium acetate, is subjected to the action of chlorine, the imino-hydrogen not being attacked. *Ethyl α-chloroglyoxylate-4-chloro-2-nitrophenylhydrazone* (V) so formed is also obtained by the action of chlorine upon *ethyl 4-chloro-2-nitrophenylazoacetoacetate* dissolved in acetic acid.



The effect of the nitro-group in the ortho-position in favouring substitution in, rather than replacement of, the acetyl group is considerably lessened by the introduction of a chlorine atom in the para-position in the phenyl nucleus. This is shown by the fact that the action of chlorine upon *o*-nitrophenylazoacetoacetate in acetic acid solution results in the formation of a mixture of the α-chloroglyoxylate and the γ-chloroacetoacetate, although 4-chloro-2-nitrophenylazoacetoacetate on similar treatment yields only the α-chloroglyoxylate.

Similarly, on treating ethyl *o*-nitrophenylazoacetoacetate with chlorine in moist chloroform solution, the γ-chloroacetoacetate is obtained, whereas 4-chloro-2-nitrophenylazo-

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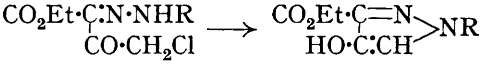
acetoacetate, on similar treatment, yields a mixture of the γ-chloroacetoacetate and the α-chloroglyoxylate.

The action of chlorine upon ethyl *m*-nitrophenylazoacetoacetate, dissolved in chloroform, causes the replacement of the acetyl group, *ethyl α-chloroglyoxylate-*m*-nitrophenylhydrazone* being formed. In acetic acid solution, with or without the addition of sodium acetate, viscous liquids were obtained from which no definite compound could be isolated.

On treatment with alcoholic ammonia the α-chloroglyoxylates yield α-aminoglyoxylates; and with alcoholic potassium acetate the γ-chloroacetoacetates lose hydrogen chloride, and ring closure takes place with the formation of 4-hydroxypyrazoles:



$$\begin{array}{l} CO_2Et\cdot C{:}N\cdot NHR \\ \quad\; CO\cdot CH_2Cl \end{array} \longrightarrow \begin{array}{l} CO_2Et\cdot C{=}N \\ \;HO\cdot C{:}CH \end{array}\!\!>\!NR$$

A theoretical discussion of these reactions is scarcely justified at the present stage, though it may be noticed that nuclear substitution, which frequently takes place in acetic acid, does not take place when chloroform is the solvent, and this may be related to the possibility of the molecules reacting in the azo- or hydrazo-form.

EXPERIMENTAL.

Under the conditions previously given (Chattaway and Ashworth, this vol., p. 475) the following have been prepared by coupling the appropriate diazonium salt with ethyl acetoacetate. *Ethyl 2-chloro-4-nitrophenylazoacetoacetate*, yellow, long, slender prisms from alcohol, m. p. 109° (Found: Cl, 11·2. $C_{12}H_{12}O_5N_3Cl$ requires Cl, 11·3%). *Ethyl 2:6-dichloro-4-nitrophenylazoacetoacetate*, yellow, slender prisms from alcohol, m. p. 104° (Found: Cl, 20·2. $C_{12}H_{11}O_5N_3Cl_2$ requires Cl, 20·4%). *Ethyl 4-chloro-2-nitrophenylazoacetoacetate*, yellow, long, slender, flattened prisms from alcohol, m. p. 127° (Found: Cl, 11·5%).

Action of Chlorine upon Ethyl p-*Nitrophenylazoacetoacetate and upon Ethyl 2-Chloro-4-nitrophenylazoacetoacetate in Acetic Acid.*—5 G. of ethyl *p*-nitrophenylazoacetoacetate (or 2-chloro-4-nitrophenylazoacetoacetate) were suspended in 20 c.c. of acetic acid and chlorine was passed for 20 minutes. On addition of water to the resulting solution *ethyl α-chloroglyoxylate-2-chloro-4-nitrophenylhydrazone* separated. It crystallised from alcohol as a labile form in pale yellow, felted, small needles which gradually redissolved whilst yellow, fragile, rhombic leaflets of the stable form separated, m. p. 120° (Found: Cl, 23·4. $C_{10}H_9O_4N_3Cl_2$ requires Cl, 23·2%).

Similarly from ethyl 2:6-dichloro-4-nitrophenylazoacetoacetate was obtained *ethyl α-chloroglyoxylate-2:6-dichloro-4-nitrophenylhydrazone*, pale yellow, long, slender, four-sided prisms from alcohol, m. p. 124° (Found: Cl, 31·4. $C_{10}H_8O_4N_3Cl_3$ requires Cl, 31·3%).

Action of Chlorine upon Ethyl p-*Nitrophenylazoacetoacetate in the Presence of Crystalline Sodium Acetate.*—5 G. of ethyl *p*-nitrophenylazoacetoacetate and 3 g. of crystallised sodium acetate were suspended in 20 c.c. of acetic acid and chlorine was passed for 20 minutes. On pouring into 200 c.c. of water, *ethyl α-chloroglyoxylate-*N*-chloro-*p*-nitrophenylhydrazone* separated as a viscous yellow solid. It crystallised from chloroform–light petroleum in bright yellow, long, slender, thin four-sided prisms, m. p. 67° [Found: Cl (added), 11·1; total Cl, 23·4. $C_{10}H_9O_4N_3Cl_2$ requires Cl (added), 11·6; total Cl, 23·2%].

Action of Chlorine upon Ethyl p-*Nitrophenylazoacetoacetate in Dry Chloroform, and Action of Aqueous Hydriodic Acid upon Ethyl α-Chloroglyoxylate-*N*-chloro-*p*-nitrophenylhydrazone.*—(1) 1 G. of ethyl *p*-nitrophenylazoacetoacetate was dissolved in dry chloroform, and chlorine passed for 10 minutes. On removal of the chloroform on a water-bath, *ethyl α-chloroglyoxylate-*p*-nitrophenylhydrazone* remained. It crystallised from acetic acid as a labile form in pale yellow, hair-like needles which gradually redissolved whilst yellow, long, flattened prisms with domed ends of the stable form separated, m. p. 192° (Found: Cl, 13·3. $C_{10}H_{10}O_4N_3Cl$ requires Cl, 13·1%).

(2) 1 G. of ethyl α-chloroglyoxylate-*N*-chloro-*p*-nitrophenylhydrazone in 10 c.c. of acetic acid was added to a solution of 1·5 g. of potassium iodide in 10 c.c. of water and 15 c.c. of acetic acid. On gentle warming, iodine was liberated and ethyl α-chloroglyoxylate-*p*-nitrophenylhydrazone separated as a yellow solid which on crystallising from acetic acid was identical with the above product.

Action of Chlorine upon Ethyl o-*Nitrophenylazoacetoacetate and Ethyl 4-Chloro-2-nitrophenylazoacetoacetate in Acetic Acid in the Presence of Sodium Acetate.*—5 G. of ethyl *o*-nitrophenylazoacetoacetate (or 4-chloro-2-nitrophenylazoacetoacetate) and 5 g. of crystallised sodium acetate were suspended in 20 c.c. of acetic acid and chlorine was passed for 20 minutes. On careful

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addition of water *ethyl α-chloroglyoxylate-4-chloro-2-nitrophenylhydrazone* separated. It crystallised from alcohol in yellow, large, lustrous plates, m. p. 108° (Found : Cl, 23·5. $C_{10}H_9O_4N_3Cl_2$ requires Cl, 23·2%).

Action of Chlorine upon Ethyl o-*Nitrophenylazoacetoacetate in Dry Chloroform.*—5 G. of ethyl *o*-nitrophenylazoacetoacetate were dissolved in 20 c.c. of dry chloroform and chlorine was passed for 20 minutes. On removal of the chloroform *ethyl* o-*nitrophenylazo-γ-chloroacetoacetate* remained. It crystallised from alcohol in yellow, long, slender, four-sided prisms, m. p. 149° (Found : Cl, 11·5. $C_{12}H_{12}O_5N_3Cl$ requires Cl, 11·3%).

Similarly from ethyl 4-chloro-2-nitrophenylazoacetoacetate was obtained *ethyl 4-chloro-2-nitrophenylazo-γ-chloroacetoacetate*, yellow, hair-like prisms from alcohol, m. p. 131° (Found : Cl, 20·6. $C_{12}H_{11}O_5N_3Cl_2$ requires Cl, 20·4%).

Action of Chlorine upon Ethyl m-*Nitrophenylazoacetoacetate.*—5 G. of ethyl *m*-nitrophenylazoacetoacetate were dissolved in 20 c.c. of chloroform and chlorine was passed for 20 minutes. On removal of the chloroform *ethyl α-chloroglyoxylate-*m-*nitrophenylhydrazone* remained as a viscous yellow solid. It crystallised from alcohol in deep yellow, compact prisms, m. p. 158° (Found : Cl, 13·3. $C_{10}H_9O_4N_3Cl$ requires Cl, 13·1%).

Formation of Ethyl p-*Nitrophenylazo-γ-chloroacetoacetate.*—2 G. of *p*-nitroaniline (1 mol.) were diazotised in 15 c.c. of concentrated hydrochloric acid with 1 g. of sodium nitrite (1 mol.) and the filtered solution was run into a cooled, well-stirred mixture of 20 g. of sodium acetate, 3 g. of ethyl γ-chloroacetoacetate (1 mol. + excess), 10 c.c. of alcohol, and 20 c.c. of water. *Ethyl* p-*nitrophenylazo-γ-chloroacetoacetate* began to separate at once. It crystallised from alcohol in pale yellow clusters of small needles, m. p. 135° (Found : Cl, 11·5. $C_{12}H_{12}O_5N_3Cl$ requires Cl, 11·3%).

In a similar manner were obtained : *Ethyl 2-chloro-4-nitrophenylazo-γ-chloroacetoacetate* from alcohol as a labile form in a pale yellow felt of minute needles, which gradually redissolved with the separation of the stable form in yellow, elongated, flattened, rectangular prisms, m. p. 134° (Found : Cl, 20·6. $C_{12}H_{11}O_5N_3Cl_2$ requires Cl, 20·4%). *Ethyl 2 : 6-dichloro-4-nitrophenylazo-γ-chloroacetoacetate* from alcohol as a labile form in yellow hair-like prisms, which gradually redissolved with the separation of the stable form in yellow, compact, rectangular prisms, m. p. 127° (Found : Cl, 28·0. $C_{12}H_{10}O_5N_3Cl_3$ requires Cl, 27·9%).

By the action of bromine upon the corresponding azoacetoacetates (*loc. cit.*) have been prepared *ethyl 2-chloro-4-nitrophenylazo-γ-bromoacetoacetate*, m. p. 130° (Found : Cl, 9·0; Br, 20·3. $C_{12}H_{11}O_5N_3ClBr$ requires Cl, 9·0; Br, 20·4%), and *ethyl 2 : 6-dichloro-4-nitrophenylazo-γ-bromoacetoacetate*, m. p. 112° (Found : Cl, 16·5; Br, 18·7. $C_{12}H_{10}O_5N_3Cl_2Br$ requires Cl, 16·6; Br, 18·7%). Both compounds form pale yellow, long, slender, flattened prisms from alcohol.

Action of Alcoholic Potassium Acetate upon Ethyl p-*Nitrophenylazo-γ-chloroacetoacetate.*—0·3 G. of potassium acetate was added to a boiling alcoholic solution of 1 g. of ethyl *p*-nitrophenylazo-γ-chloroacetoacetate. The solution darkened in colour and 4-hydroxy-3-carbethoxy-1-(4′-nitrophenyl)pyrazole separated as a yellow solid. It crystallised from acetic acid in colourless hair-like needles, m. p. 220°, identical in all respects with the compound obtained by the action of potassium acetate upon ethyl *p*-nitrophenylazo-γ-bromoacetoacetate (Chattaway and Ashworth, *loc. cit.*).

In a similar manner were prepared *4-hydroxy-3-carbethoxy-1-(2′-chloro-4′-nitrophenyl)pyrazole*, colourless, long, slender, four-sided prisms from alcohol, m. p. 188° (Found : Cl, 11·3. $C_{12}H_{10}O_5N_3Cl$ requires Cl, 11·35%), and *4-hydroxy-3-carbethoxy-1-(2′ : 6′-dichloro-4′-nitrophenyl)-pyrazole*, colourless, compact, rectangular prisms from alcohol, m. p. 197° (Found : Cl, 20·3. $C_{12}H_9O_5N_3Cl_2$ requires Cl, 20·5%).

*Ethyl α-Aminoglyoxylate-*p-*nitrophenylhydrazone.*—This was obtained by stirring ethyl α-chloroglyoxylate-*p*-nitrophenylhydrazone into a saturated solution of alcoholic ammonia. It crystallised from aqueous alcohol in yellow, long, slender prisms, m. p. 181°, identical in all respects with the product obtained by similar treatment of ethyl α-bromoglyoxylate-*p*-nitrophenylhydrazone (*loc. cit.*). Similarly were obtained : *ethyl α-aminoglyoxylate-2 : 6-dichloro-4-nitrophenylhydrazone*, yellow, long, hair-like prisms from alcohol, m. p. 182° (Found : Cl, 22·3. $C_{10}H_{10}O_4N_4Cl_2$ requires Cl, 22·1%); *ethyl α-aminoglyoxylate-4-chloro-2-nitrophenylhydrazone*, red rhombic plates from alcohol, m. p. 141° (Found : Cl, 12·2. $C_{10}H_{11}O_4N_4Cl$ requires Cl, 12·4%), and *ethyl α-aminoglyoxylate-*m-*nitrophenylhydrazone*, yellow, slender, flattened prisms from alcohol, m. p. 158° (Found : N, 22·2. $C_{10}H_{12}O_4N_4$ requires N, 22·2%).

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