132. *Derivatives of* 4 : 5-*Diketopyrazoline.*

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In continuation of previous work on the influence of halogen atoms on ring closure in the diketopyrazoline series (J., 1927, 1323) the action of 2 : 5-di- and 2 : 4 : 5-tri-chlorophenylhydrazine upon dihydroxytartaric acid and oxalacetic ester has been studied.

When 2 : 5-dichlorophenylhydrazine acts upon dihydroxytartaric acid, an osazone, *diketosuccinic acid* 2 : 5-*dichlorophenylosazone* (I), is formed. On crystallisation from acetic acid or from acetic anhydride it yields exclusively *diketosuccinic anhydride* 2 : 5-*dichlorophenylosazone*.

$$\begin{matrix}(HO)_2C\cdot CO_2H \\ (HO)_2C\cdot CO_2H\end{matrix} \longrightarrow \underset{\text{(I.)}}{\begin{matrix}C_6H_3Cl_2\cdot NH\cdot N{:}C\cdot CO_2H \\ C_6H_3Cl_2\cdot NH\cdot N{:}C\cdot CO_2H\end{matrix}} \xrightarrow[HCl]{EtOH} C_6H_3Cl_2\cdot N\!<\!\begin{matrix}N{=}C\cdot CO_2Et \\ CO\cdot C{:}N\cdot NH\cdot C_6H_3Cl_2\end{matrix}$$

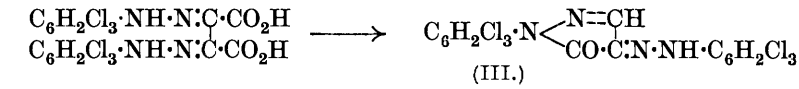
(II.)

Acidification of the sodium salt of the osazone by hydrochloric acid does not bring about ring closure, but when the osazone or its anhydride is boiled with an alcoholic solution of hydrogen chloride *ethyl* 4 : 5-*diketo*-1-(2′ : 5′-*dichlorophenyl*)*pyrazoline*-3-*carboxylate* 4-(2″ : 5″-*dichlorophenylhydrazone*) (II) is formed.

The substance (II) can also be obtained from oxalacetic ester, which, in the presence of sodium acetate, couples with 2 : 5-dichlorobenzenediazonium chloride to give *ethyl diketosuccinate* 2 : 5-*dichlorophenylhydrazone*. This condenses with 2 : 5-dichlorophenylhydrazine and gives the corresponding *osazone* (as I), from which (II) is obtained by heating with alcoholic hydrogen chloride. On hydrolysis the ester (II) gives the *pyrazolonecarboxylic acid*.

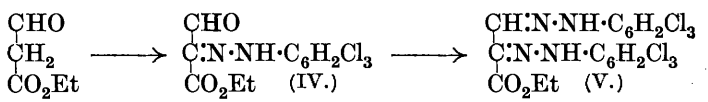
In the same way *ethyl diketosuccinate* 2 : 4 : 5-*trichlorophenylosazone* is prepared by coupling 2 : 4 : 5-trichlorobenzenediazonium chloride with oxalacetic ester and condensing the product with 2 : 4 : 5-trichlorophenylhydrazine. The corresponding *diketosuccinic acid* 2 : 4 : 5-*trichlorophenylosazone* is prepared from dihydroxytartaric acid and trichlorophenylhydrazine.

The introduction of a third chlorine atom into each nucleus considerably diminishes the solubility of these compounds. Although diketosuccinic acid 2 : 4 : 5-trichlorophenylosazone is easily converted into its *anhydride*, neither it nor its ester readily undergoes pyrazolone ring closure, which can be brought about only under conditions which cause the elimination of the carboxyl group, with formation of 4 : 5-*diketo*-1-(2′ : 4′ : 5′-*trichlorophenyl*)*pyrazoline*-4-(2″ : 4″ : 5″-*trichlorophenylhydrazone*) (III).



(III.)

That ring closure occurs prior to the elimination of the carboxyl group is made probable by the stability of *carbethoxyglyoxal*-2 : 4 : 5-*trichlorophenylosazone* (V), obtained by coupling 2 : 4 : 5-trichlorobenzenediazonium chloride with formylacetic ester and condensing the resulting *hydrazone* (IV) with 2 : 4 : 5-trichlorophenylhydrazine.



(IV.) (V.)

This osazone can be recovered unchanged after prolonged heating with alcoholic hydrogen chloride or acetic anhydride. It cannot satisfactorily be hydrolysed to the corresponding acid owing to marked decomposition when heated with alkali, but *carboxyglyoxal*-2 : 4 : 5-*trichlorophenylosazone* (as V) is readily obtained by con-

densing dibromopyruvic acid with 2 : 4 : 5-trichlorophenylhydrazine and similarly does not undergo pyrazolone ring closure.

EXPERIMENTAL.

Diketosuccinic Acid 2 : 5-*Dichlorophenylosazone* (I).—A solution of 3 g. of sodium dihydroxytartrate (1 mol.) in 14 c.c. of equal parts of concentrated hydrochloric acid and water was added to a solution of 5 g. of 2 : 5-dichlorophenylhydrazine hydrochloride (2 mols.) in 200 c.c. of water. The mixture was stirred for 5 hours and finally heated to 80°. *Diketosuccinic acid* 2 : 5-*dichlorophenylosazone*, which separated as a yellow solid, was washed with boiling water and dried at 110° (yield, 5 g.); m. p. 195° (decomp.). It cannot be crystallised unchanged (Found : Cl, 30·6. $C_{16}H_{10}O_4N_4Cl_4$ requires Cl, 30·6%).

When the acid (2·4 g.) was dissolved in 30 c.c. of boiling acetic anhydride, a deep red solution was obtained, from which, on cooling, *diketosuccinic anhydride* 2 : 5-*dichlorophenylosazone* separated quantitatively as orange hair-like needles, m. p. 233° (Found : Cl, 31·9. $C_{16}H_8O_3N_4Cl_4$ requires Cl, 31·8%).

Diketosuccinophenylhydrazide 2 : 5-*dichlorophenylosazone*, obtained quantitatively from the corresponding anhydride (2 g.) and phenylhydrazine (1 g.) in boiling acetic acid (30 c.c.), crystallised from xylene, in which it was sparingly soluble, as hair-like orange-brown needles, m. p. 286° (Found : Cl, 26·4. $C_{22}H_{14}O_2N_6Cl_4$ requires Cl, 26·5%).

Ethyl 4 : 5-*Diketo*-1-(2′ : 5′-*dichlorophenyl*)*pyrazoline*-3-*carboxylate* 4-(2″ : 5″-*Dichlorophenylhydrazone*) (II).—(a) 3·3 G. of diketosuccinic acid 2 : 5-dichlorophenylosazone (or its anhydride) were boiled for 4 hours with 25 c.c. of alcohol saturated with dry hydrogen chloride. A yellow solution was obtained, from which, on cooling, the *hydrazone* (II) separated as a yellow crystalline solid. It crystallised from acetic acid, in which it was moderately easily soluble, as thin orange-yellow plates, m. p. 213° (Found : Cl, 29·7. $C_{18}H_{12}O_3N_4Cl_4$ requires Cl, 29·9%).

(b) A solution of 5 g. of 2 : 5-dichloroaniline in 8 c.c. of acetic acid and 24 c.c. of concentrated hydrochloric acid was diazotised below 0° by 2·5 g. of sodium nitrite in 10 c.c. of water. The filtered solution was added drop by drop to an ice-cold mixture of 1·8 g. of ethyl oxalacetate, 50 g. of crystalline sodium acetate, and 100 c.c. of water. *Ethyl diketosuccinate* 2 : 5-*dichlorophenylhydrazone*, which slowly separated (4·5 g.), crystallised from light petroleum, in which it was moderately easily soluble, as golden-yellow plates, m. p. 101° (Found : Cl, 19·7. $C_{14}H_{14}O_5N_2Cl_2$ requires Cl, 19·7%).

When 0·8 g. of this hydrazone, dissolved in a little alcohol, was added to a hot alcoholic solution of 0·5 g. of 2 : 5-dichlorophenyl-

hydrazine hydrochloride, *ethyl diketosuccinate* 2 : 5-*dichlorophenylosazone* separated as a yellow solid. It crystallised from light petroleum, in which it was sparingly soluble, as small crystalline nodules, m. p. 207° (Found : Cl, 27·1. $C_{20}H_{18}O_4N_4Cl_4$ requires Cl, 27·3%). When the osazone was boiled with alcoholic hydrogen chloride, and the solution cooled, the pyrazolone (II), identical with that obtained in (a), separated as small yellow plates.

4 : 5-*Diketo*-1-(2′ : 5′-*dichlorophenyl*)*pyrazoline*-3-*carboxylic acid* 4 (2″ : 5″-*dichlorophenylhydrazone*) (as II) was obtained quantitatively when 1·3 g. of the ester (II) were boiled with 100 c.c. of 10% aqueous sodium hydroxide for 7 hours and the cooled mixture acidified by hydrochloric acid. It crystallised from acetic acid, in which it was moderately easily soluble, as short orange prisms, m. p. 214° (decomp.) (Found : Cl, 31·9. $C_{16}H_8O_3N_4Cl_4$ requires Cl, 31·9%).

Diketosuccinic Acid 2 : 4 : 5-*Trichlorophenylosazone.*—A solution of 3·6 g. of 2 : 4 : 5-trichlorophenylhydrazine hydrochloride in 100 c.c. of hot water was rapidly cooled to produce small crystals. The subsequent treatment with sodium dihydroxytartrate (1·6 g. in 20 c.c. of concentrated hydrochloric acid and 20 c.c. of water) was that described for the preparation of the dichloro-compound. *Diketosuccinic acid* 2 : 4 : 5-*trichlorophenylosazone* separated quantitatively as a red solid which decomposed when heated and could not be crystallised without partial conversion into the anhydride (Found : Cl, 40·6. $C_{16}H_8O_4N_4Cl_6$ requires Cl, 40·0%).

When the acid (5·2 g.) was boiled with acetic anhydride (50 c.c.) for ¼ hour, it was converted into the *anhydride*, which crystallised from xylene, in which it was sparingly soluble, as deep orange plates (4·7 g.), m. p. 295—300° (Found : Cl, 41·0. $C_{16}H_6O_3N_4Cl_6$ requires Cl, 41·3%).

Ethyl Diketosuccinate 2 : 4 : 5-*Trichlorophenylosazone.*—5 G. of trichloroaniline in 10 c.c. of acetic acid and 30 c.c. of concentrated hydrochloric acid were diazotised below 0°, with 2 g. of sodium nitrite in 10 c.c. of water. The filtered solution was slowly run into an ice-cold well-stirred mixture of 5·1 g. of ethyl oxalacetate, 70 c.c. of alcohol, and 50 g. of crystalline sodium acetate. Ethyl diketosuccinate 2 : 4 : 5-trichlorophenylhydrazone separated as a reddish solid which could not be obtained crystalline and so was immediately converted into the osazone, 3·4 g. being boiled with 2·5 g. of 2 : 4 : 5-trichlorophenylhydrazine hydrochloride in 25 c.c. of alcohol. On cooling, *ethyl diketosuccinate* 2 : 4 : 5-*trichlorophenylosazone* separated as a brown solid. It crystallised from boiling toluene, in which it was readily soluble, as yellowish-brown plates with a faint blue reflex; m. p. 224° (yield, 3·5 g.) (Found : Cl, 36·1. $C_{20}H_{16}O_4N_4Cl_6$ requires Cl, 36·2%).

4 : 5-*Diketo*-1-(2′ : 4′ : 5′-*trichlorophenyl*)*pyrazoline*-4-(2″ : 4″ : 5″-*trichlorophenylhydrazone*) (III).—2·9 G. of diketosuccinic anhydride (or acid or ester) 2 : 4 : 5-trichlorophenylosazone were heated with 20 c.c. of alcohol, saturated with dry hydrogen chloride, in a sealed tube at 130° for 9 hours. On cooling, the pyrazoline *derivative* (III) separated: after being washed with chloroform to remove a little decomposition product, it crystallised from boiling xylene, in which it was sparingly soluble, as orange-coloured, hair-like, felted needles, m. p. 308—310° (decomp.) (Found: Cl, 45·3; N, 12·2. $C_{15}H_6ON_4Cl_6$ requires Cl, 45·2; N, 11·9%).

Carbethoxyglyoxal-2 : 4 : 5-*trichlorophenylhydrazone* (IV).—3·9 G. of 2 : 4 : 5-trichloroaniline in 20 c.c. of concentrated hydrochloric acid were diazotised below 0° by 1·5 g. of sodium nitrite in 10 c.c. of water, and the filtered solution was dropped into a well-stirred ice-cold mixture of 4·0 g. of sodioformylacetic ester (prepared by the action of ethyl formate upon ethyl acetate in the presence of sodium, in dry ether; compare Wislicenus, *Ber.*, 1887, **20**, 2931), 100 c.c. of water, and 30 g. of crystalline sodium acetate. *Carbethoxyglyoxal*-2 : 4 : 5-*trichlorophenylhydrazone* separated as a yellow viscid solid, which was extracted with chloroform, the solution dried over sodium sulphate, and the chloroform evaporated on the water-bath. On cooling, the dark viscid mass soon solidified. It crystallised from alcohol, in which it was readily soluble, as brownish-yellow, small, irregular plates (6·1 g.), m. p. 118° (Found: Cl, 32·5. $C_{11}H_9O_3N_2Cl_3$ requires Cl, 32·8%).

Carbethoxyglyoxal-2 : 4 : 5-*trichlorophenylosazone* (V).—To a solution of 2·1 g. of trichlorophenylhydrazine hydrochloride in 40 c.c. of boiling alcohol, 2·8 g. of carbethoxyglyoxal-2 : 4 : 5-trichlorophenylhydrazone in 15 c.c. of hot alcohol were added. *Carbethoxyglyoxal*-2 : 4 : 5-*trichlorophenylosazone*, which separated at once, crystallised from xylene, in which it was moderately easily soluble, as felted yellow needles (3·1 g.), m. p. 242° (Found: Cl, 41·3. $C_{17}H_{12}O_2N_4Cl_6$ requires Cl, 41·2%).

Carboxyglyoxal-2 : 4 : 5-*trichlorophenylosazone* (as V).—When 2·5 g. of dibromopyruvic acid, dissolved in a little cold alcohol, were added to an alcoholic solution of 5 g. of 2 : 4 : 5-trichlorophenylhydrazine hydrochloride, *carboxyglyoxal*-2 : 4 : 5-*trichlorophenylosazone* separated, and was collected after 10 minutes' heating on the water-bath. It crystallised from nitrobenzene, in which it was easily soluble, as a felted mass of slender orange-yellow prisms, m. p. 284° (Found: Cl, 43·6; N, 11·4. $C_{15}H_8O_2N_4Cl_6$ requires Cl, 43·5; N, 11·4%).

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