

CLXXXV.—*The Action of Halogen-substituted Phenylhydrazines upon Dihydroxytartaric Acid.*

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THE action of hydrazines upon dihydroxytartaric acid was first studied by Ziegler and Locher (*Ber.*, 1887, **20**, 834), but many of their conclusions were later shown to be incorrect. Repetition of their work by Knorr (*Ber.*, 1888, **21**, 1201), Anschutz (*Annalen*, 1896, **294**, 219), and Gnehm and Benda (*Annalen*, 1897, **299**, 100) showed that the nature of the product depends upon the substituents in the nucleus; thus ordinary phenylhydrazine gives the expected osazone, while phenylhydrazine-*p*-sulphonic acid gives a pyrazolone derivative (tartrazine). The unsubstituted osazone may be converted into a pyrazolone derivative corresponding to tartrazine by crystallisation from acetic acid. Gnehm and Benda (*loc. cit.*) made the further important observation that, when this osazone is crystallised from acetic anhydride, water is lost in a second manner giving an acid anhydride isomeric with the pyrazolone derivative.

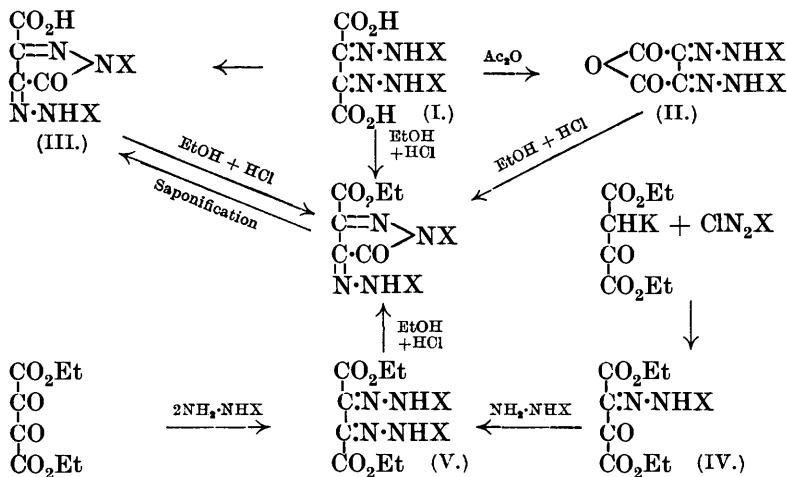
In the present paper, the influence of halogen substituents in the phenyl residues upon the ease of formation from the osazones of the pyrazolone and anhydride ring systems is described. The compounds thus obtained are similar in properties to the corresponding unsubstituted compounds, the accumulation of halogen in the phenyl groups being attended only by a diminishing solubility and a greater tendency towards formation of the anhydride in preference to the pyrazolone.

The osazones are sparingly soluble substances which cannot be crystallised unchanged from any solvent. On heating with acetic anhydride or benzoyl chloride, they are converted into deep red anhydrides. These anhydrides are unaffected by prolonged boiling with water, but dissolve in warm aqueous sodium carbonate to give solutions of the disodium salts of the osazones. On heating with alcohols containing hydrogen chloride, esters of the isomeric pyrazolone acids are formed.

The osazones are converted into hydrazones of diketopyrazoline-carboxylic acids by crystallisation from acetic acid or by acidification of their sodium salts. In the former reaction, varying amounts of the isomeric anhydrides are simultaneously produced. These pyrazoline derivatives are sparingly soluble, yellow or orange-yellow solids which undergo esterification only with difficulty. Their esters are more easily obtained from the corresponding osazone or anhydride.

The structure of the pyrazolone derived from the 2 : 4-dibromophenylosazone has been confirmed by two syntheses.

The following scheme represents the reactions with 2 : 4-dibromophenylosazone, X denoting  $C_6H_3Br_2$  :



#### EXPERIMENTAL.

*Preparation of Sodium Dihydroxytartrate.*—Finely powdered tartaric acid (200 g.) is suspended in 280 c.c. of nitric acid ( $d$  1.42) and 500 c.c. of concentrated sulphuric acid are added slowly with constant stirring. The temperature rises to about  $70^\circ$  and a clear solution is obtained which is covered over and allowed to cool slowly for 8—12 hours. The semi-solid pulp of tartaric acid dinitrate thus obtained is broken up, and freed from acid as completely as possible by suction and pressure; during this operation the mass should be protected from atmospheric moisture. The hard-pressed, solid mass is stirred with crushed ice until it dissolves, ice-water being added if necessary. The liquid is nearly neutralised with sodium carbonate and, after addition of a litre of saturated sodium acetate solution, filtered and left in a cool place for 2—3 days; at first colourless, it becomes green, owing to the liberation of oxides of nitrogen, and finally colourless when these have escaped. Sodium dihydroxytartrate separates as a very sparingly soluble, white powder, which is filtered off, washed with cold water, and dried by exposure to air.

*Preparation of Halogen-substituted Phenylhydrazines.*—The reduction of the diazonium salts with stannous chloride, the method previously described for the preparation of the mono- and di-halogen-

substituted phenylhydrazines, is not altogether satisfactory on a large scale on account of the cost of the materials and the difficulty of completely removing the tin from the products. The following modification of Fischer's method of reduction with sodium sulphite gives much better results.

A suspension of the finely powdered amine ( $\frac{1}{3}$  g.-mol.) in 70 c.c. of concentrated hydrochloric acid (excess) is warmed to about 60° for 1 hour to convert the amine into its hydrochloride, and is then cooled in a freezing mixture, and an ice-cold solution of sodium nitrite (20 g. in 50 c.c. of water) is added, with vigorous stirring, during not less than 1 hour. The diazonium solution is filtered and added slowly to a solution of sodium sulphite, prepared by passing sulphur dioxide into a solution of 45 g. of sodium hydroxide in 300 c.c. of water until an acid reaction is just indicated by phenolphthalein. (An excess of sulphur dioxide must be avoided; otherwise tarry matters are produced on addition of the diazonium solution and the yield of hydrazine is greatly diminished.) The resulting bright orange solution is warmed to 60°, and made acid to litmus by the addition of concentrated hydrochloric acid (about 20 c.c.); the colour then changes to pale yellow. The solution is heated for about an hour, 100 c.c. of concentrated hydrochloric acid are added, and the mixture is allowed to cool. The hydrazine hydrochloride crystallises as a pulp of small needles, which are filtered off and recrystallised from dilute hydrochloric acid (1 : 4). The yield of the air-dried product is 80—90% of the theoretical.

*Diketosuccinic acid 2 : 4-dibromophenylosazone* (I) was prepared by adding a solution of 26 g. of sodium dihydroxytartrate (1 mol.) in 180 c.c. of moderately concentrated hydrochloric acid (1 : 1) to a fine suspension of 60 g. of 2 : 4-dibromophenylhydrazine hydrochloride (2 mols.) in 1500 c.c. of very dilute hydrochloric acid (1 : 100). The mixture was stirred for 6 hours and afterwards heated at 80° for 2 hours. The *osazone*, which separated as a soft, orange-coloured powder, was filtered off without previous cooling, repeatedly washed with boiling water, and dried at 110°. It was thus obtained as an orange powder, m. p. 205° (decomp.) (Found: Br, 50.1.  $C_{16}H_{10}O_4N_4Br_4$  requires Br 49.8%).

*Anhydrodiketosuccinic Acid 2 : 4-Dibromophenylosazone* (II).—The *osazone* (I) was added to boiling acetic anhydride until no more would dissolve. A clear, deep red solution was thus obtained which on cooling deposited the *anhydride* in large, red, elongated prisms, m. p. 267° (decomp.) (Found: Br, 51.35.  $C_{16}H_8O_3N_4Br_4$  requires Br, 51.3%).

1-2' : 4'-*Dibromophenyl-4 : 5-diketopyrazoline-3-carboxylic acid*  
4-2'' : 4''-*dibromophenylhydrazone* (III) is formed together with the

isomeric anhydride (II) on crystallising the osazone (I) from acetic acid. The two isomerides are readily distinguished owing to their marked difference in colour and crystalline form. Their separation by crystallisation from acetic acid, although difficult on account of their sparing solubility, can be effected as follows: A saturated, boiling solution, during cooling to 70°, deposits most of (III) together with some of the anhydride; below this temperature, the anhydride continues to separate with only a small amount of the pyrazolone. By repeating the process with each of the two fractions the substances are obtained pure.

The compound (III) is, however, best obtained by acidifying the deep brown solution produced by boiling its ethyl ester (see below) (5 g.) for 4 hours with 200 c.c. of 10% sodium hydroxide solution; the orange-yellow powder thus obtained separates from acetic acid in clusters of minute, orange-yellow crystals, m. p. 248° (decomp.) (Found: Br, 51.4.  $C_{16}H_8O_3N_4Br_4$  requires Br, 51.3%).

The *methyl* ester of the acid (III) is best obtained by heating the anhydride (II) in a sealed tube with methyl alcohol, containing 2% of dry hydrogen chloride, for 8 hours at 100°. It is moderately easily soluble in acetic acid, from which it separates in very small, orange-yellow needles, m. p. 233° (Found: Br, 50.2.  $C_{17}H_{10}O_3N_4Br_4$  requires Br, 50.2%). The *ethyl* ester, obtained by boiling the osazone (I), the anhydride (II), or the pyrazolone (III) with alcohol containing 5% of dry hydrogen chloride, crystallises from acetic acid, in which it is moderately easily soluble, in long, slender, yellow prisms, m. p. 229° (Found: Br, 49.0.  $C_{18}H_{12}O_3N_4Br_4$  requires Br, 49.1%). The *n-butyl* ester, which is similarly prepared, is easily soluble in acetic acid, from which it separates in yellow, glistening plates, m. p. 175° (Found: Br, 47.0.  $C_{20}H_{16}O_3N_4Br_4$  requires Br, 47.1%).

*Ethyl diketosuccinate 2:4-dibromophenylhydrazone* (IV) is not readily obtained pure from ethyl diketosuccinate owing to the simultaneous formation of the osazone. It is, however, readily prepared from ethyl oxalacetate. A cold aqueous solution of 2:4-dibromobenzene-diazonium chloride is added slowly and with vigorous stirring to an aqueous solution of the potassium derivative of ethyl oxalacetate, cooled in a freezing mixture. A sticky red mass separates from which, by repeated crystallisation from alcohol, the *hydrazone* is obtained in small, pale yellow, compact prisms, m. p. 95° (Found: Br, 35.4.  $C_{14}H_{14}O_5N_2Br_2$  requires Br, 35.55%).

*Ethyl diketosuccinate 2:4-dibromophenyllosazone* (V) cannot be prepared by the direct esterification of the osazone (I) on account of simultaneous pyrazolone formation. It is obtained by the action in alcoholic solution (1) of dibromophenylhydrazine upon the mono-

hydrazone, (2) of excess of dibromophenylhydrazine upon ethyl diketosuccinate. It separates from alcohol in glistening, yellow, four-sided plates, m. p. 197° (Found : Br, 45.9.  $C_{20}H_{18}O_4N_4Br_4$  requires Br, 45.8%). On boiling with alcohol containing hydrogen chloride, it is converted into the ethyl ester of (III), m. p. 229°, described above.

*Diketosuccinic acid p-bromophenylosazone* (I; X =  $C_6H_4Br$ ) was obtained as a soft, orange-red powder, m. p. 201° (decomp.) (Found : Br, 33.2.  $C_{16}H_{12}O_4N_4Br_2$  requires Br, 33.1%).

The *anhydride* (formula as II) forms deep red, compact prisms, m. p. 262° (decomp.) (Found : Br, 34.4.  $C_{16}H_{10}O_3N_4Br_2$  requires Br, 34.3%). This and all the following compounds, unless otherwise stated, are moderately easily soluble in acetic acid, from which they were crystallised.

*1-p-Bromophenyl-4 : 5-diketopyrazoline-3-carboxylic acid 4-p-bromophenylhydrazone* (formula as III) is sparingly soluble in acetic acid, from which it separates in very small, compact, yellow prisms, m. p. 260° (decomp.) (Found : Br, 34.5.  $C_{16}H_{10}O_3N_4Br_2$  requires Br, 34.3%).

Its *methyl* ester, which is best obtained by heating the osazone anhydride in a sealed tube with methyl alcohol, containing 2% of dry hydrogen chloride, for 8 hours at 100°, forms long, thin, orange prisms, m. p. 213° (Found : Br, 33.5.  $C_{17}H_{12}O_3N_4Br_2$  requires Br, 33.3%). The *ethyl* ester forms thin, orange-yellow prisms, m. p. 191° (Found : Br, 32.5.  $C_{18}H_{14}O_3N_4Br_2$  requires Br, 32.4%).

*Diketosuccinic acid 2 : 4-dichlorophenylosazone* (I; X =  $C_6H_3Cl_2$ ) was obtained as a soft, orange-red powder, m. p. 198° (decomp.) (Found : Cl, 30.9.  $C_{16}H_{10}O_4N_4Cl_4$  requires Cl, 30.6%).

The *anhydride* (formula as II) forms small, elongated, red prisms, m. p. 242° (decomp.) (Found : Cl, 31.9.  $C_{16}H_8O_3N_4Cl_4$  requires Cl, 31.8%).

*1-2' : 4'-Dichlorophenyl-4 : 5-diketopyrazoline-3-carboxylic acid 4-2'' : 4''-dichlorophenylhydrazone* (formula as III) is sparingly soluble in acetic acid, from which it separates in nodular aggregates of very small, yellow needles, m. p. 252° (decomp.) (Found : Cl, 31.7.  $C_{16}H_8O_3N_4Cl_4$  requires Cl, 31.8%).

Its *ethyl* ester forms long, fine needles, m. p. 212° (Found : Cl, 29.9.  $C_{18}H_{12}O_3N_4Cl_4$  requires Cl, 29.95%).

*Diketosuccinic acid p-chlorophenylosazone* (I; X =  $C_6H_4Cl$ ) was obtained as a soft, orange-red powder, m. p. 195° (decomp.) (Found : Cl, 17.7.  $C_{16}H_{12}O_4N_4Cl_2$  requires Cl, 18.0%).

The *anhydride* (formula as II) forms small, slender, red prisms, m. p. 257° (decomp.) (Found : Cl, 18.9.  $C_{16}H_{10}O_3N_4Cl_2$  requires Cl, 18.8%).

1 - p - Chlorophenyl-4 : 5-diketopyrazoline-3-carboxylic acid 4 - p - chlorophenylhydrazone (formula as III) is obtained by crystallising the osazone from acetic acid. It is rather sparingly soluble in acetic acid, from which it separates in small, orange-yellow, compact prisms, m. p.  $254^{\circ}$  (decomp.) (Found : Cl, 18.8.  $C_{16}H_{10}O_3N_4Cl_2$  requires Cl, 18.8%).

Its ethyl ester forms very slender, orange-yellow prisms, m. p.  $190^{\circ}$  (Found : Cl, 17.7.  $C_{18}H_{14}O_3N_4Cl_2$  requires Cl, 17.5%).

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[Received, March 30th, 1927.]

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