XL.—*An Investigation into the Formation of 4(5)-Aminoglyoxalines. Part I.*

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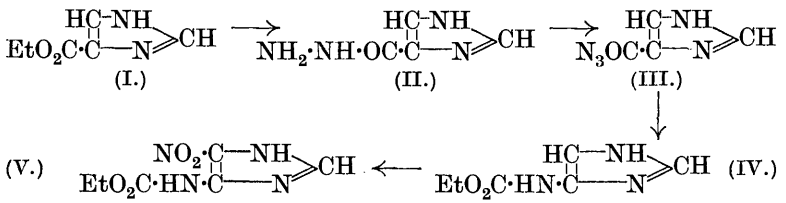
THE only evidence at present (Fargher, J., 1920, **117**, 668; Pyman, J., 1922, **121**, 2616) that 4(5)-aminoglyoxalines are true aromatic amines is the formation, after diazotisation, of coloured solutions with aqueous sodium β-naphthoxide. In order to submit examples of them to typical reactions characteristic of aromatic amines, it seemed desirable to commence a detailed study of their formation and stability. They have hitherto been prepared by the reduction of 4(5)-nitroglyoxalines and 4(5)-benzeneazoglyoxalines (Fargher and Pyman, J., 1919, **115**, 235; Windaus and Langenbeck, *Ber.*, 1923, **56**, 685).

Reduction of 4(5)-nitro-2-methyl- and of 4(5)-nitro-glyoxalines with iron and water (and a drop of acetic acid), ferrous sulphate

and sodium hydroxide, sodium sulphide, or activated aluminium or by West's method, (J., 1925, **127**, 494) gave no basic material; the dark blue solutions mentioned by previous workers were, however, often obtained. (Catalytic hydrogenation is under investigation.)

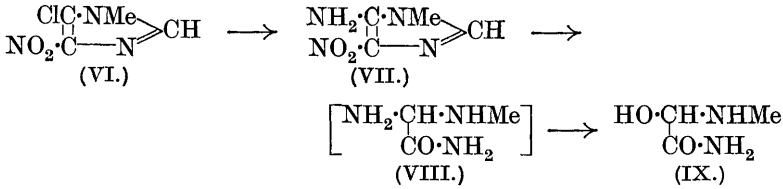
The present communication deals mainly with the application of the Curtius synthesis of amines to ethyl glyoxaline-4(5)-carboxylate (I). When this ester is heated with hydrazine hydrate, *glyoxaline*-4(5)-*carboxyhydrazide* (II) is obtained, which is converted by treatment with nitrous acid into *glyoxaline*-4(5)-*carboxyazide* (III): this compound, heated with ethyl alcohol on the water-bath, yields 4(5)-*carbethoxyaminoglyoxaline* (IV). Similarly, with methyl alcohol, the *carbomethoxyamino*-derivative can be prepared.



Attempts to convert the azide by boiling with water into the *s*-carbamide failed: the solution gave an intense Pauly reaction, but an amorphous picrate only could be isolated. The carbomethoxy- and carbethoxy-amino-derivatives were recovered to the extent of about 30% and 50% respectively after boiling with hydrochloric acid, and attempts to obtain 4(5)-aminoglyoxaline by heating them with 2*N*-hydrochloric acid in a sealed tube at 150° or with concentrated sulphuric acid on the water-bath were likewise unsuccessful. Satisfactory hydrolysis also could not be effected with 10% aqueous sodium carbonate or boiling 2*N*-sodium hydroxide. The phthalimido-derivative, which might be quantitatively hydrolysed to the amine (compare Ing and Manske, J., 1926, 2348), could not be prepared. The *as*-carbamide was not formed when the carbethoxyamino-derivative was heated with 3·5% alcoholic ammonia at 150°. 4(5)-*Nitro*-5(4)-*carbethoxyaminoglyoxaline* (V), notwithstanding the presence of a nitro-group in the *o*-position with respect to the substituted amino-group, also could not be converted by hydrolysis with 10% aqueous sodium carbonate into the corresponding amine.

Balaban and Pyman (J., 1924, **125**, 1565) and Sarasin and Wegmann (*Helv. Chim. Acta*, 1924, **7**, 713) have shown that the halogen atom in 5-chloro-4-nitro-1-methylglyoxaline (VI) can be replaced by the sulpho- and the cyano-group. The compound does not react with aqueous ammonia or acetamide, but when it is heated

with 3·5% alcoholic ammonia at 140° 4-*nitro*-5-*amino*-1-*methylglyoxaline* (VII) is obtained in good yield. This amine does not form an acetyl or a benzylidene derivative, but after treatment with nitrous acid it gives with alkaline β-naphthol a greenish-blue insoluble dye and with alkaline resorcinol a violet solution, whereas with sodium hydroxide only a pale yellow colour is obtained. The amine is rapidly decomposed by 16% hydrochloric acid (or even 7%) at room temperature, nitrous acid being liberated and a compound, m. p. 140°, formed: this is presumably *α-methylamino-α-hydroxyacetamide* (IX), because when it is boiled with aqueous sodium hydroxide it yields ammonia and methylamine. Owing to the



mild conditions of hydrolysis, fission occurs at the 1 : 2- and the 2 : 3-positions of (VII), formic acid being split off [compare the formation of dibenzoyldiaminoethylene from glyoxaline (Bamberger and Berle, *Ber.*, 1892, **25**, 278) and of *dl*-alanine-*N*-methylamidine from 5-amino-1 : 4-dimethylglyoxaline (Pyman, *loc. cit.*)]. The substance (VIII) is then acted upon by the liberated nitrous acid, hydroxyl being substituted for the amino-group. The formation of glyoxylic acid on alkaline hydrolysis of the amide (IX), and its subsequent conversion into glycollic acid, must be presumed, for the only identifiable acid obtained was oxalic acid. As Böttinger (*Annalen*, 1879, **198**, 217) has shown that ammonium α-amino-α-hydroxyacetate is decomposed by boiling water, the possibility of obtaining the acid corresponding to (IX) and its conversion directly into methylamine and glyoxylic acid was very remote.

EXPERIMENTAL.

For the preparation of glyoxaline-4(5)-carboxylic acid (Fargher and Pyman, *loc. cit.*; Balaban and Pyman, J., 1922, **121**, 954) it is unnecessary to isolate the carboxyanilide. After removal of unchanged glyoxaline-4 : 5-dicarboxylic acid, the acid solution is concentrated to 25 c.c. and treated with concentrated hydrochloric acid (250 c.c.); 50 g. of the dicarboxylic acid give about 20 g. of glyoxaline-4(5)-carboxylic acid.

Glyoxaline-4(5)-*carboxyhydrazide* (II).—When a mixture of 5·6 g. of ethyl glyoxaline-4(5)-carboxylate and hydrazine hydrate (4·0 c.c.; 2 mols.) was heated on the water-bath, solution took place in 15

minutes; after a further 15 minutes, when the solution was cooled, the *hydrazide* (5·0 g.), m. p. 210°, separated in almost quantitative yield. It crystallised from boiling water, in which it was fairly readily soluble, in long, colourless, silky needles containing $1H_2O$, m. p. 213° (Found for air-dried substance: loss at 100°, 12·5, 12·8. $C_4H_6ON_4,H_2O$ requires H_2O, 12·5%. Found in dried material: N, 45·1, 43·6; C, 37·9; H, 4·9. $C_4H_6ON_4$ requires N, 44·4; C, 38·1; H, 4·8%). The hydrazide is moderately easily soluble in alcohol but insoluble in benzene, chloroform, and ether. It reduces ammoniacal silver nitrate slowly, but not Fehling's solution.

The *picrate* crystallises from water (1 in 85 parts of boiling water) in anhydrous yellow needles, m. p. 223° (decomp.) (Found in air-dried salt by nitron estimation: picric acid, 64·8.

$$C_4H_6ON_4,C_6H_3O_7N_3$$

requires picric acid, 64·5%).

Glyoxaline-4(5)-carboxyazide (III).—A mixture of the hydrazide (6·3 g.), concentrated hydrochloric acid (7·0 c.c.), and a little ice was treated at 0° with sodium nitrite (7·0 g. in 15 c.c. of water). After 15 minutes, the *azide* was collected and washed with ice-water, 8·0 g. of slightly moist material, decomp. 137° (explosively), being obtained [Found in material dried at 100°: N (Dumas), 51·1. $C_4H_3ON_5$ requires N, 51·0%]. It crystallised from 95% alcohol in minute stout rods.

When the azide is heated with water on the water-bath, gas is evolved and a dark green solution is produced, from which a *picrate* can be obtained; this chars at 230° after previous darkening (Found in dried material: picric acid, 66·4. $C_7H_8ON_6,2C_6H_3O_7N_3$ requires picric acid, 69·4%). Attempts to regenerate the base from the picrate were unsuccessful.

4(5)-*Carbethoxyaminoglyoxaline* (IV).—The azide (6·3 g.) was heated under reflux with absolute ethyl alcohol (50 c.c.) for 4 hours, the solvent removed, the residue dissolved in a little dilute hydrochloric acid and treated with charcoal, and the filtered solution concentrated to a few c.c. and basified with anhydrous sodium carbonate; the *carbethoxyamino*-derivative (3·0 g.; yield, 42·2%) obtained crystallised from boiling water, in which it was readily soluble, in anhydrous, colourless, hexagonal plates, m. p. 180° (Found in dried material: N, 27·2. $C_6H_9O_2N_3$ requires N, 27·1%). It is very soluble in alcohol, moderately easily soluble in benzene, sparingly in chloroform, but insoluble in ether. With Pauly's reagent it gives a deep red solution. The hydrochloride regenerated from the picrate was obtained as a gum, which did not crystallise.

The *picrate* crystallises from boiling water (1 in 60 parts) in anhydrous, golden, hexagonal, prismatic needles, decomp. 210°

(sintering from 203°) (Found in substance dried at 100° : picric acid, 59·6, 59·8. $C_6H_9O_2N_3$,$C_6H_3O_7N_3$ requires picric acid, 59·6%).

The *nitrate* crystallises from water, in which it is moderately easily soluble, in anhydrous, colourless, hexagonal prisms, decomp. 143° (Found in salt dried at 100° : nitric acid, by nitron method, 29·1. $C_6H_9O_2N_3$,HNO_3 requires nitric acid, 28·9%).

4(5)-*Carbomethoxyaminoglyoxaline*, similarly prepared from the azide and methyl alcohol (yield, about 50%), crystallises from water (1 in 8 parts, boiling) in anhydrous diamond-shaped plates, m. p. 175° (Found in material dried at 100° : N, 30·3. $C_5H_7O_2N_3$ requires N, 29·8%). It is very soluble in alcohol, sparingly soluble in ether, and insoluble in benzene and chloroform. With Pauly's reagent, a rich port-wine colour is produced. The *picrate* crystallises from water, in which it is sparingly soluble, in anhydrous irregular prisms, which blacken at about 240° and decompose at 243° (Found : picric acid, 61·4, 61·6. $C_5H_7O_2N_3$,$C_6H_3O_7N_3$ requires picric acid, 61·9%).

5(4)-*Nitro*-4(5)-*carbethoxyaminoglyoxaline* (V).—The preceding nitrate (1 g.) was added to concentrated sulphuric acid (2 c.c.) at 0° during 10 minutes and then warmed on the water-bath until effervescence began (10 minutes). The *nitro*-derivative, which separated (yield, 58%) when the mixture was poured on ice, crystallised from water in large, anhydrous, rhomboidal plates, m. p. 234° (decomp.) (Found in material dried at 100° : N, 28·3. $C_6H_8O_4N_4$ requires N, 28·0%). It is soluble to the extent of 1 in 400 parts of boiling water and also in hot alcohol, but insoluble in benzene, chloroform, and ether. No colour reaction is given with Pauly's reagent.

4-*Nitro*-5-*amino*-1-*methylglyoxaline* (VII).—5-Chloro-4-nitro-1-methylglyoxaline (6·6 g.) and alcoholic ammonia (3·5%; 90 c.c.) were heated together at 140° for 4 hours. The *nitro*-compound, which had separated (3·7 g.; yield, 63·7%), crystallised from water (solubility, 1 part in 170 parts, boiling) in yellow, anhydrous, rectangular plates, m. p. 303° (decomp.) (Found in material dried at 100° : C, 33·7; H, 4·3; N, 39·8. $C_4H_6O_2N_4$ requires C, 33·8; H, 4·2; N, 39·4%). It is soluble in concentrated hydrochloric acid, but not in dilute acid, alcohol, chloroform, or ether. It dissolves in boiling glacial acetic acid, forming apparently an acetate, for when the diluted solution is treated successively with sodium nitrite and alkaline β-naphthol a greenish-blue colour is obtained. The nitro-compound does not give a picrate when treated with aqueous picric acid.

Action of cold 16% *hydrochloric acid.* When the nitro-compound (2·6 g.) was added to 16% hydrochloric acid (10·4 c.c.) and stirred,

the solution darkened considerably and after some minutes much heat was evolved, the temperature rose from 21° to 47°, effervescence ensued, nitrous acid was liberated, and crystals immediately separated (1·1 g.), leaving a mother-liquor (M). The solid did not give a Pauly reaction, or a coloured solution with sodium β-naphthoxide after treatment with nitrous acid. When it was recrystallised from a little water (10 c.c.; charcoal), a small crop (0·1 g.), m. p. 140°, was obtained; the mother-liquor on concentration gave only a dark brown gum. The mother-liquor (M) on concentration gave 0·3 g., m. p. 140°. The combined mother-liquors were mixed with an excess of aqueous sodium hydroxide, and the volatile amines distilled into hydrochloric acid. After evaporation, the residue gave 0·5 g. insoluble in absolute alcohol (Found: Cl, 64·8. Calc. for NH_4Cl: Cl, 66·4%) and 0·6 g., m. p. 195—200°, soluble in absolute alcohol (Found: Cl, 53·5. Calc. for NH_2Me,HCl: Cl, 52·6%). The alkaline solution yielded, after acidification and treatment with calcium chloride in ammoniacal solution, 0·4 g. containing 97% of calcium oxalate.

α-Methylamino-α-hydroxyacetamide (IX) is moderately easily soluble in hot water, but much less so in cold, and crystallises in long, anhydrous, pale brown needles, m. p. 140°. Its aqueous solution is neutral to litmus (Found in material dried at 100°: C, 34·0; H, 7·8; N, 26·7, 27·0. $C_3H_8O_2N_2$ requires C, 34·6; H, 7·7; N, 26·9%).

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