Orientation of the nitro- and arylazo-glyoxalines. Fission of the glyoxaline nucleus / by Robert George Fargher.

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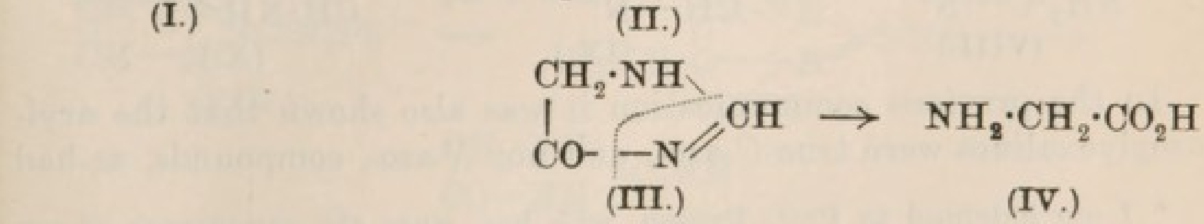
LXX.—*Orientation of the Nitro- and Arylazo-glyoxalines. Fission of the Glyoxalone Nucleus.*

By Robert George Fargher.

In the course of a recent communication (T., 1919, **115**, 217), the author, in conjunction with Prof. F. L. Pyman, showed that the nitro-group, on entering the glyoxaline nucleus, takes up the 4- or 5-position.[*] Subsequent reduction with tin and hydrochloric acid, undertaken with the object of examining the corresponding amino-glyoxalines and determining directly the orientation of the nitro-group, led to fission of the nucleus, two of the three nitrogen atoms appearing in the form of ammonia. It was suggested that the first stage of the disintegration was probably the elimination of the amino-group as ammonia with formation of a glyoxalone, certain members of the purine group—also derivatives of 4-amino-glyoxaline—having been shown to undergo hydrolysis in this manner (compare Tafel and Meyer, *Ber.*, 1908, **41**, 2546; Biltz, *Ber.*, 1910, **43**, 1589). It was therefore of interest to investigate the reduction in more detail with the objects (1) of determining directly the orientation of the nitro-group, (2) of establishing the transformation into the glyoxalone, and (3) of studying the fission of the simple glyoxalone nucleus under the influence of acids. The earlier experiments had shown that the products of complete reduction, apart from ammonium chloride, the predominant constituent, were very uninviting in appearance. Consequently, treatment in cold hydrochloric acid solution with just sufficient stannous chloride to reduce the nitro-group was employed, with success. Nitro-glyoxaline, in addition to ammonia, yielded glycine, as did also nitro-2-methylglyoxaline, whilst nitro-5-methylglyoxaline yielded α-alanine. This clearly demonstrates that the nitroglyoxalines are correctly formulated as 4-nitro-derivatives, that the reduction is followed by hydrolysis of the 4-aminoglyoxaline (II), with the


(I.) (II.) (III.) (IV.)

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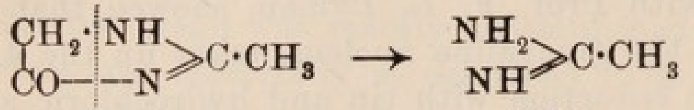
[*] In glyoxalines containing a free imino-group the 4- and 5-positions are equivalent.

formation of the 4-glyoxalone (III), and that one fission of the 4-glyoxalone nucleus takes place between the 1:2- and 3:4-positions. This fission recalls the isolation of sarcosine,

$$NHMe\cdot CH_2\cdot CO_2H,$$

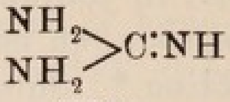
by Rosengarten and Strecker (*Annalen*, 1871, **157**, 1) as a product of hydrolysis of caffeine by baryta.

The reduction of nitro-2-methylglyoxaline gave evidence of a second mode of fission, as α-amino-α-iminoethane (VI) was isolated.



$$\begin{matrix}CH_2\cdot NH\\ CO-\!-N\end{matrix}\!>\!C\cdot CH_3 \rightarrow \begin{matrix}NH_2\\ NH\end{matrix}\!>\!C\cdot CH_3$$

(V.) (VI.)



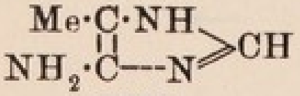
$$\begin{matrix}NH_2\\ NH_2\end{matrix}\!>\!C\!:\!NH$$

(VII.)

Fission therefore takes place between the 1:5- and 3:4-positions (V), presumably with simultaneous formation of glycollic acid, and reveals the probable mechanism of the formation of guanidine (VII) in the reduction of 2-benzeneazoglyoxaline.

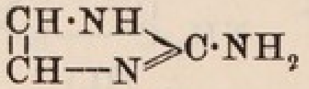
What is practically the reverse process was accomplished by Finger (*J. pr. Chem.*, 1907, [ii], **76**, 93), who condensed α-imino-α-ethoxyethane with the ethyl ester of glycine, and obtained 2-methyl-4-glyoxalone.

In neither of these reductions was the aminoglyoxaline obtained. Consequently, the isolation of a small and variable proportion of 4-*amino*-5-*methylglyoxaline* (VIII) from the reduction of 4-nitro-5-methylglyoxaline was both unexpected and important, and permitted comparison of a simple 4-aminoglyoxaline with the 2-aminoglyoxaline isolated in the earlier work (*loc. cit.*, pp. 223, 246). It was already evident that they evinced a considerable difference in stability, and the dissimilarity extends to most of the other properties. Whilst 2-aminoglyoxaline (IX) is a monacidic base, which does not yield a benzylidene derivative, does not react with sodium-β-naphthoxide after treatment with nitrous acid,* and, in brief, behaves in many of its reactions as if it existed in the tautomeric form (X), 4-amino-5-methylglyoxaline reacts as a true aromatic amine, forming a *dihydrochloride* and a crystalline *benzylidene* derivative, and coupling readily with sodium-β-naphthoxide after treatment with nitrous acid.



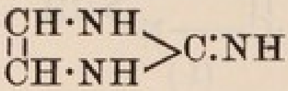
$$\begin{matrix}Me\cdot C\cdot NH\\ \|\\ NH_2\cdot C-\!-N\end{matrix}\!>\!CH$$

(VIII.)



$$\begin{matrix}CH\cdot NH\\ \|\\ CH-\!-N\end{matrix}\!>\!C\cdot NH_2$$

(IX.)



$$\begin{matrix}CH\cdot NH\\ \|\\ CH\cdot NH\end{matrix}\!>\!C\!:\!NH$$

(X.)

In the previous communication it was also shown that the arylazoglyoxalines were true *C*-azo-, and not *N*-azo-, compounds, as had

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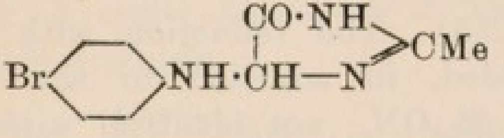
* I am indebted to Prof. Pyman, who has, since the appearance of our joint communication, made a further study of the 2-aminoglyoxalines, for this correction (compare *loc. cit.*, p. 248).

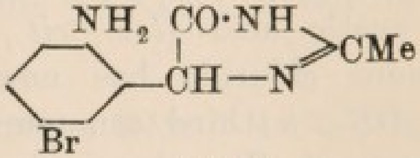
been suggested by Rung and Behrend (*Annalen*, 1892, **271**, 28) and Burian (*Ber.*, 1904, **37**, 696). Whilst, however, in the case of the 2-arylazoglyoxalines this was established by a study of their reduction products, proof of the constitution of the 4-arylazo-derivatives was mainly indirect. On complete reduction, they behaved like the nitroglyoxalines, the ring undergoing fission, whilst their general properties were antagonistic to the supposition that they were 1-arylazo-derivatives.

As the results now obtained with the nitroglyoxalines indicated the course the reaction might be expected to take, it was evident that the formation of glyoxalone derivatives in the reduction of the 4-arylazoglyoxalines would definitely determine the orientation of the arylazo-group.

The reduction of *p*-bromobenzeneazo-2-methylglyoxaline and 4-benzeneazo-5-methylglyoxaline was therefore undertaken under the same conditions as had been successful in the case of the nitroglyoxalines. The former, which, previously, had yielded only *p*-bromoaniline and ammonia as isolable reduction products, readily gave a *glyoxalone*, for which there were two possible formulæ (XI, XII).

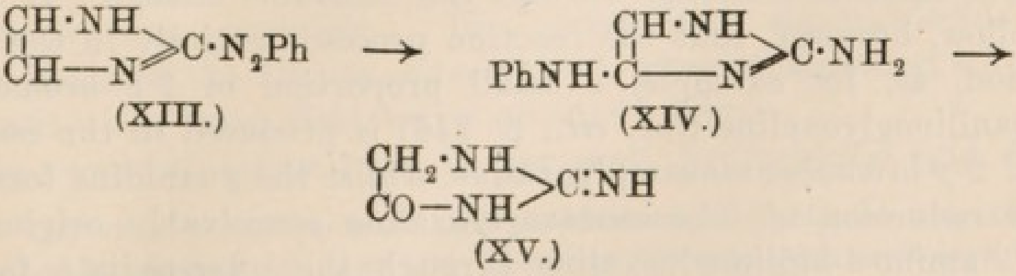


(XI.)



(XII.)

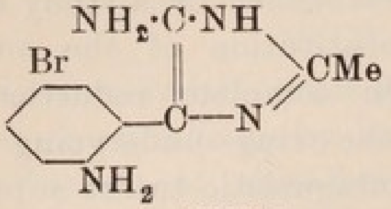
The formation of a *benzylidene* derivative similar to that obtained from 2-amino-4-*p*-aminophenylglyoxaline shows the second of these to be correct. The failure, therefore, of the compound to give more than a faint yellow colour with sodium-β-naphthoxide after treatment with nitrous acid is interesting. The comparative stability towards hydrochloric acid serves to confirm the constitution, as an earlier stage in the formation of glycocyamidine (XV) and alacreatinine from 2-benzeneazoglyoxaline (XIII) and 2-benzeneazo-5-methylglyoxaline respectively, by reduction with zinc and acetic acid, is no doubt represented by 2-amino-4-anilinoglyoxaline (XIV) and 2-amino-4-anilino-5-methylglyoxaline, which then undergo hydrolysis and rearrangement.

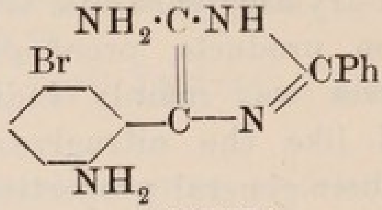


$$\left.\begin{matrix}CH\cdot NH\\ \|\\ CH-N\end{matrix}\right\rangle C\cdot N_2Ph \rightarrow PhNH\cdot\left.\begin{matrix}CH\cdot NH\\ \|\\ C-\!\!-N\end{matrix}\right\rangle C\cdot NH_2 \rightarrow \left.\begin{matrix}CH_2\cdot NH\\ |\\ CO-NH\end{matrix}\right\rangle C{:}NH$$

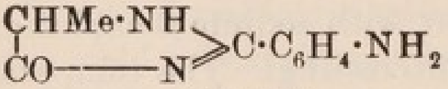
(XIII.) (XIV.) (XV.)

Practically the whole of the reduction product appeared in the form of an insoluble stannichloride, probably that of 5-*amino-4-(2′-amino-5′-bromophenyl)-2-methylglyoxaline* (XVI), as, after


(XVI.)

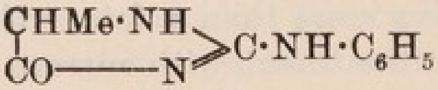

(XVII.)

conversion into the hydrochloride, roughly molecular proportions of ammonium chloride and the glyoxalone were obtained on fractionation. It is therefore permissible to assume that the constitution of the reduction product of bromobenzeneazo-2-phenylglyoxaline (*loc. cit.*, p. 258) is correctly represented as 5-*amino-4-(2′-amino-5′-bromophenyl)-2-phenylglyoxaline* (XVII), the product evincing a greater stability towards acids than the corresponding 2-methyl derivative. The further study of the reduction of 4-benzeneazo-5-methylglyoxaline was of interest, as two products of undetermined constitution had already been isolated, a base $C_9H_{10}ON_2$, from the reduction with tin and hydrochloric acid (*loc. cit.*, p. 254), and a base, $C_{10}H_{11}ON_3$, from the reduction with zinc and acetic acid (*loc. cit.*, p. 255). The reduction with cold stannous chloride has now yielded, in addition to the base, $C_9H_{10}ON_2$, a third compound, $C_{10}H_{11}ON_3$, not identical with the product of the zinc reduction. It gave a *dihydrochloride*, a *benzylidene* derivative, and, after treatment with nitrous acid, coupled with sodium-β-naphthoxide, and is therefore 2-p-*aminophenyl-5-methyl-4-glyoxalone* (XVIII).



$$\left.\begin{array}{l}\mathrm{CHMe{\cdot}NH} \\ \mathrm{CO}\text{———}\mathrm{N}\end{array}\right>\mathrm{C{\cdot}C_6H_4{\cdot}NH_2}$$

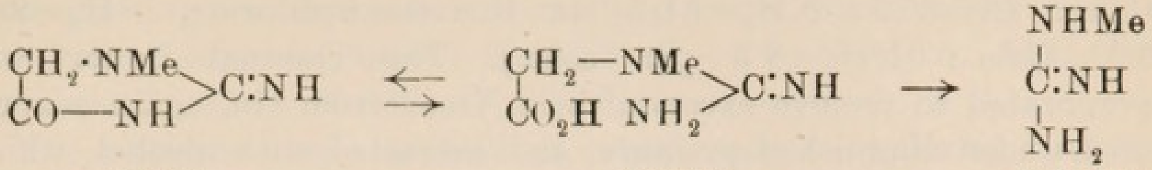
(XVIII.)



$$\left.\begin{array}{l}\mathrm{CHMe{\cdot}NH} \\ \mathrm{CO}\text{———}\mathrm{N}\end{array}\right>\mathrm{C{\cdot}NH{\cdot}C_6H_5}$$

(XIX.)

The base from the zinc reduction was monacidic, did not couple, and did not react with benzaldehyde, and is therefore 2-*anilino-5-methyl-4-glyoxalone* (XIX). It is of interest to record that the reactions which have been examined so far indicate that the zinc and acetic acid reduction favours the semidine change, whilst the stannous chloride reduction favours the benzidine change. It does not follow, however, that the reaction proceeds entirely in the one direction, as, for example, a small proportion of 2-5′-bromo-2′-aminoanilinoglyoxaline (*loc. cit.*, p. 246) is produced in the reduction of 2-*p*-bromobenzeneazoglyoxaline, whilst the guanidine formed in the reduction of 2-benzeneazoglyoxaline conceivably originates from 2-amino-4-anilinoglyoxaline through the intermediate formation of glycocyamidine. This is of interest in view of the close relationship of creatine (XXI) to creatinine (XX) and the suggestion that the former is the precursor of methylguanidine (XXII)

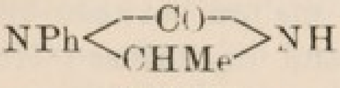


$$\left.\begin{matrix}CH_2\cdot NMe\\ \vert\\ CO—NH\end{matrix}\right\rangle C{:}NH \quad \overset{\longleftarrow}{\longrightarrow} \quad \left.\begin{matrix}CH_2—NMe\\ \vert\\ CO_2H\ \ NH_2\end{matrix}\right\rangle C{:}NH \quad \longrightarrow \quad \begin{matrix}NHMe\\ \vert\\ C{:}NH\\ \vert\\ NH_2\end{matrix}$$

(XX.) (XXI.) (XXII.)

in the organism (Achelis, *Zeitsch. physiol. Chem.*, 1906, **50**, 10).

Neither of the modes of fission established in the simple glyoxalone nucleus accounts for the formation of the base, $C_9H_{10}ON_2$, from either 2-*p*-aminophenyl-5-methyl-4-glyoxalone or 2-anilino-5-methyl-4-glyoxalone, one of which probably represents an earlier stage in its formation. It is difficult to avoid the supposition that fission ensues between the 4:5- and 2:3-positions, the reaction being conditioned by the presence of the *p*-aminophenyl or anilino-grouping in the 2-position. The small amount of these substances available has rendered it impossible, so far, to examine their hydrolytic products in detail, but it is worth noting that in the former case the properties of the base necessitate the assumption of subsequent ring-formation involving the *p*-amino-group, whilst, in the latter, a cyclic derivative of carbamide (XXIII) is one of the possible products.



$$NPh\left\langle\begin{matrix}-\!-CO-\!-\\ CHMe\end{matrix}\right\rangle NH$$

(XXIII.)

$$NHPh\cdot CO\cdot NH\cdot CHMe\cdot NH\cdot CO\cdot NHPh$$

(XXIV.)

Attempts to synthesise this by the condensation of acetal or acetaldehyde with phenylcarbamide led, however, solely to *ethylidenebisphenylcarbamide* (XXIV).

EXPERIMENTAL.

Reduction of 4-Nitroglyoxaline. Formation of Glycine and Ammonia.

To 33 grams of nitroglyoxaline, dissolved in 100 c.c. of concentrated hydrochloric acid, 175 c.c. of stannous chloride solution* were gradually added, the temperature being maintained below 5° and the mixture stirred mechanically for some time after the addition was complete. The crystalline stannichloride was collected, and the filtrate concentrated, when it deposited a further quantity, the total yield being about 49 grams.

On recrystallisation from 10 per cent. hydrochloric acid, it was

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* The stannous chloride solution used throughout the investigation was prepared by mixing 40 grams of stannous chloride with sufficient hydrochloric acid to form 100 c.c. of solution.

obtained in large, octahedral masses, which, after removal of tin, gave solely ammonium chloride (Found: Cl=66·1; NH_3=31·6. Calc.: Cl=66·3; NH_3=31·8; in the stannichloride, NH_3=9·1, 9·2. Calc.: NH_3=9·3 per cent.). The residual liquor was evaporated to remove excess of acid, freed from tin, again evaporated under diminished pressure, and extracted with alcohol, which left undissolved 6·3 grams of ammonium chloride. The syrupy alcoholic extract, on solution in water and addition of picric acid, yielded only traces of an insoluble picrate, 60 grams of nitroglyoxaline giving 0·5 gram in a pure condition. This separated from water in well-defined needles, which darkened rapidly above 200° and melted at 234° (corr.), and gave analytical figures in fair agreement with *aminoglyoxaline dipicrate*, but the amount was too small to permit of its further examination (Found: C=32·8; H=2·6; N=22·8. $C_3H_5N_3,2C_6H_3O_7N_3$ (541·2) requires C=33·3; H=2·1; N=23·3 per cent.). The residual solution was reconverted into the hydrochloride, evaporated to dryness in a vacuum, dissolved in alcohol, and submitted to fractionation. There first deposited a further 1·0 gram of ammonium chloride, then (*a*) 5·2 grams melting at about 174°, (*b*) 3·1 grams melting at about 156°, and (*c*) 2·8 grams melting between 130° and 140°. Further crops were obtained more readily from the mother liquor after the addition of alcoholic hydrogen chloride, and these melted between 130° and 140°. Crops (*a*) and (*b*) were united and crystallised from rather less than their own weight of water, when, on keeping, there separated 4 grams of large, flattened prisms melting at 189° (corr.), sintering some degrees earlier. This substance proved to be the sesquihydrochloride of glycine (Found: C=25·5; H=6·1; N=14·9; Cl=19·1. $(C_2H_5O_2N)_2,HCl$ requires C=25·7; H=5·9; N=15·0; Cl=19·0 per cent.). The mother liquor, on further concentration, deposited a mixture of this hydrochloride and the normal hydrochloride of glycine, from which the latter was obtained on crystallisation in presence of excess of hydrochloric acid. It separated as a serrated mass of somewhat hygroscopic, flattened prisms, which melted at 182° (corr.), sintering above 150° (Found: C=21·7; H=5·7; N=12·7; Cl=31·2. $C_2H_5O_2N,HCl$ requires C=21·5; H=5·4; N=12·6; Cl=31·8 per cent.). Crop (*c*), and subsequent crops melting at about the same temperature, were mixed and recrystallised from alcohol, when a mass of fine, silky needles, melting at 145° (corr.) and showing no depression when mixed with a synthetic specimen of glycine ethyl ester hydrochloride, was obtained (Found: C=34·5; H=7·4; N=10·0; Cl=25·0. $C_4H_9O_2N,HCl$ requires C=34·4; H=7·2; N=10·0; Cl=25·4 per cent.).

The identity was further established by the isolation of glycine from all three hydrochlorides, the glycine melting at 247° (corr.) and showing no depression of melting point when mixed with a synthetic specimen (Found: C=31·8; H=6·9; N=18·5. $C_2H_5O_2N$ requires C=32·0; H=6·7; N=18·7 per cent.).

The ultimate alcoholic residues, which were very dark in colour, gave no further crystalline material.

Reduction of 4-Nitro-2-methylglyoxaline. Formation of Glycine, α-Amino-α-iminoethane, and Ammonia.

The reduction of 12·7 grams of nitro-2-methylglyoxaline was carried out as in the previous instance. There were first obtained 7·6 grams of ammonium stannichloride. The more soluble stannichlorides were converted into hydrochlorides in the customary manner, the solution evaporated to dryness under diminished pressure, and extracted with alcohol, leaving 3·5 grams of practically pure ammonium chloride. The alcoholic extract was concentrated to a syrup, dissolved in 50 c.c. of water, and treated with a boiling solution of 13 grams of picric acid in 250 c.c. of water, when 7·7 grams of a crude picrate were obtained. This, on recrystallisation from water, separated in glistening, orange prisms sintering from 245° and melting at 252° (corr.). The yield amounted to 3·6 grams. 2·8 Grams of this picrate were converted into the hydrochloride, excess of hydrochloric acid being avoided. The resulting aqueous solution was evaporated to dryness under diminished pressure, below 50°, leaving a solid residue, which was dissolved in a little alcohol and kept. There gradually separated long, colourless, prismatic needles, which melted at 174° (corr.), and proved to be the hydrochloride of α-amino-α-iminoethane (VI, p. 669). Pinner (*Ber.*, 1884, **17**, 178; "Die Iminoäther," p. 107) gives the melting point as 165° or 166—167° (Found: C=25·7; H=7·5; N=29·1; Cl=36·5. $C_2H_6N_2,HCl$ requires C=25·4; H=7·5; N=29·6; Cl=37·5 per cent.).

The melting point of the picrate is given by Dieckmann (*Ber.*, 1892, **25**, 547) as 247° (Found: C=33·8; H=3·3; N=23·9. $C_2H_6N_2,C_6H_3O_7N_3$ requires C=33·4; H=3·2; N=24·4 per cent.).

The identity of the base was further established by the preparation of the *aurichloride*. This salt crystallises from water in fern-shaped clusters of golden-yellow needles, which melt at 266° and are anhydrous.

Found: Au=49·2.

$C_2H_6N_2,HCl,AuCl_3$ (398·1) requires Au=49·5 per cent.

The platinichloride, previously described by Pinner, separates from water in small, orange, flattened prisms or in large, red, flattened prisms, according to the rate of crystallisation. Like the aurichloride, it is anhydrous. It melts at 242° (corr.) (Found: Pt=37·0. $(C_2H_6N_2)_2$,2HCl,$PtCl_4$ requires Pt=37·1 per cent.).

The residual liquor from the separation of the α-amino-α-iminoethane picrate was regenerated into the hydrochloride and evaporated to dryness, leaving a dark syrup. As this showed no tendency to crystallise, it was dissolved in absolute alcohol containing hydrogen chloride, warmed for a short time on the water-bath, and concentrated, when, on keeping, glycine ethyl ester hydrochloride gradually separated, and was identified by comparison with the synthetic product and by analysis (Found: N=10·0; Cl=25·1. $C_4H_9O_2N$,HCl requires N=10·0; Cl=25·4 per cent.).

The residue from the glycine ester hydrochloride yielded no further crystalline material. A small quantity of a non-nitrogenous ester was isolated, but the amount was too small to attempt its purification and identification.

Reduction of Nitro-5-methylglyoxaline. Formation of α-Alanine, 4-Amino-5-methylglyoxaline, and Ammonia.

The reduction of 11 grams of 4-nitro-5-methylglyoxaline was carried out as in the previous instances, yielding 7·5 grams of ammonium stannichloride and 1·4 grams of ammonium chloride. The syrupy, alcoholic extract was dissolved in 25 c.c. of water and treated with a boiling solution of 8 grams of picric acid in 200 c.c. of water, when there quickly separated 4 grams of fine needles contaminated with oily matter. On keeping overnight, a further 2 grams separated, mainly picric acid, and the mother liquor deposited picric acid only on concentration. The two crops were crystallised from alcohol, from which there separated clusters of long, old-gold needles, which blackened rapidly above 180° and melted and decomposed at 195° (corr.).

The picrate was converted into the hydrochloride, excess of acid being avoided. The solution, on evaporation in a vacuum at as low a temperature as possible, left a syrup, which became crystalline on mixing with a few drops of alcohol. The *hydrochloride* separates from alcohol in minute, colourless prisms, which melt at 189° (corr.) and are anhydrous. The crystallisation should be conducted as quickly as possible, as the alcoholic solution decomposes on keeping.

Found: C=28·2; H=5·6; N=24·2; Cl=41·0.

$C_4H_7N_3$,2HCl (170·0) requires C=28·2; H=5·3; N=24·7; Cl=41·7 per cent.

The solution of the hydrochloride reduces ammoniacal silver nitrate strongly on warming. It gives, with sodium nitroprusside on addition of sodium hydroxide, a brown colour; with sodium diazobenzene-*p*-sulphonate in sodium carbonate solution, a bright yellow colour; on treatment with nitrous acid and addition to sodium-β-naphthoxide, a deep reddish-brown solution; with ferric chloride, no colour; with Fehling's solution, reduction on warming; with potassium permanganate in cold acid solution, instant reduction; with gold chloride, a brown precipitate which dissolves on warming, reduction taking place.

The properties and composition indicate that the substance is correctly formulated as *4-amino-5-methylglyoxaline* (VIII, p. 669).

The *picrate* is sparingly soluble in water, but more readily so in alcohol, from which it separates in old-gold needles, which darken rapidly above 180° and melt at 195° (corr.).

Found: $N = 25{\cdot}3$.

$C_4H_7N_3,C_6H_3O_7N_3$ (326·2) requires $N = 25{\cdot}8$ per cent.

The *benzylidene* derivative was prepared by treating 0·23 gram of the hydrochloride in 5 c.c. of water with 0·4 gram of sodium acetate and 0·2 c.c. of benzaldehyde. On shaking vigorously, a solid product gradually formed. This was collected and washed with water and ether, in which it is sparingly soluble. It dissolves readily in alcohol, but less so in ethyl acetate, from which it separates in clusters of well-defined needles, which are anhydrous and melt and decompose at 217° (corr.), gradually darkening in colour above 190°.

Found: $N = 22{\cdot}9$.

$C_{11}H_{11}N_3$ (185·2) requires $N = 22{\cdot}7$ per cent.

The residual liquor from the separation of the 4-amino-5-methylglyoxaline picrate was reconverted into the hydrochloride and evaporated to dryness, when it left about 3 grams of a semi-solid mass, which yielded only ammonium chloride (1·0 gram) on crystallisation from water or alcohol. It was dissolved in water therefore, chlorine determined in an aliquot portion, and the hydrochloric acid in the remainder removed by the addition of the calculated quantity of freshly precipitated silver carbonate. The resulting solution was evaporated to a syrup, mixed with a little alcohol, and kept, when α-alanine gradually separated. This melted, without recrystallisation, at 287° (corr.), a synthetic specimen melting at the same temperature in the same bath, and the mixture of the two showing no depression. The identity was further confirmed by its reactions, analysis, and formation of the copper salt (Found: C=40·1; H=8·1; N=15·4. $C_3H_7O_2N$ requires C=40·4; H=7·9; N=15·7 per cent.).

Strecker (*Annalen*, 1850, **75**, 36) found that the air-dried copper salt retained one molecule of water of crystallisation. More recently, Zelinsky and Stadnikoff (*Ber.*, 1908, **41**, 2062) failed to confirm this, and described a salt with three molecules of water of crystallisation. Both the acid obtained above and a synthetic specimen of undoubted purity yielded a copper salt with only one molecule of water of crystallisation (Found: Cu = 24·7. $(C_3H_6O_2N)_2Cu,H_2O$ requires Cu=24·7 per cent.), and the salt did not gain appreciably in weight on keeping for several days in an atmosphere saturated with moisture.

Reduction of 4-p-*Bromobenzeneazo-2-methylglyoxaline.*

13·2 Grams of bromobenzeneazo-2-methylglyoxaline were triturated with 120 c.c. of cold hydrochloric acid and gradually treated with 72 c.c. of stannous chloride solution, the trituration being continued and the temperature maintained below 10°. The insoluble stannichloride which gradually formed was collected, and the residual liquor freed from tin and evaporated, leaving only 0·3 gram of residue, in which ammonia and *p*-bromoaniline were identified. The insoluble stannichloride was dissolved in water, freed from tin, and the resulting solution evaporated to low bulk, when, on keeping, a quantity of minute needles separated. These dissolved readily in water, but more sparingly in 10 per cent. hydrochloric acid, from which they were obtained in clusters of glistening, elongated, rhombic prisms melting at 273° (corr.).

Found: C=38·9, 39·6; H=3·9, 3·9; N=13·65.

0·2031 gave 0·2178 AgCl+AgBr, 0·2208 being required.

$C_{10}H_{10}ON_3Br,HCl$ (304·55) requires C=39·4; H=3·65; N=13·8 per cent.

The corresponding *base* is precipitated as a mass of minute, colourless needles on treating the concentrated aqueous solution of the hydrochloride with a molecular proportion of sodium hydroxide. It decomposes in warm aqueous solution or on exposure to the air. Dried at 60° in a vacuum, it appears to retain a molecule of water of crystallisation.

Found: C=42·1, 42·3; H=4·4, 4·5; N=14·2; Br=27·8.

$C_{10}H_{10}ON_3Br,H_2O$ (286·1) requires C=41·95; H=4·2; N=14·7; Br=27·9 per cent.

The solution of the base gives no coloration with sodium diazobenzene-*p*-sulphonate in sodium carbonate solution. After treatment with nitrous acid in acid solution, a pale yellow colour develops on addition to sodium-β-naphthoxide. An ammoniacal solution of silver nitrate is reduced in the cold. With Fehling's solution, a bluish-green precipitate is formed, which becomes dark green on warming. With sodium nitroprusside in presence of sodium hydroxide, a reddish-brown colour develops, which changes to green on acidification with acetic acid, and is discharged by excess of the reagent. The aqueous solution reduces cold aqueous acid permanganate. The base reacts with benzaldehyde, with formation of a *benzylidene* derivative, which was not obtained in a crystalline condition. The properties and composition of the base point, therefore, to its being 2-*methyl*-4-(2′-*amino*-5′-*bromophenyl*)-5-*glyoxalone* (XII, p. 670).

The *picrate* separates from water in glistening, orange plates which, when dried in the air, melt at 157° (corr.), sintering slightly above 140°. It appears to contain two molecules of water of crystallisation, one of which is lost on drying at 60° in a vacuum.

Found: in air-dried material, $N = 15{\cdot}65$; loss at 60° in a vacuum $= 3{\cdot}4$. In dried material, $N = 16{\cdot}2$.

$C_{10}H_{10}ON_3Br,C_6H_3O_7N_3,2H_2O$ requires $N = 15{\cdot}8$. For loss of $1H_2O$, $H_2O = 3{\cdot}4$ per cent.

$C_{10}H_{10}ON_3Br,C_6H_3O_7N_3,H_2O$ (515·1) requires $N = 16{\cdot}3$ per cent.

After the separation of most of the above hydrochloride, ammonium chloride began to deposit, and a careful fractionation of the mixture revealed that the two products were present in approximately molecular proportions.

Reduction of 4-Benzeneazo-5-methylglyoxaline.

3·7 Grams were triturated with 20 c.c. of hydrochloric acid and treated, as in the previous experiment, with 12 c.c. of stannous chloride solution. The insoluble stannichlorides amounted to 6·8 grams of moist material. Tin was removed, and the resulting solution evaporated under diminished pressure to low bulk, when the hydrochloride of the base, $C_9H_{10}ON_2$ (*loc. cit.*, p. 254), separated, about 1·8 grams being obtained. The mother liquors eventually deposited ammonium chloride, and, on suitable treatment, yielded a small amount of aniline. The more soluble stannichlorides, when treated similarly, yielded a second *hydrochloride*, which separated as a matted mass of minute needles, readily soluble in water but sparingly so in alcohol. After recrystallisation from 10 per cent. hydrochloric acid, it darkened, but did not melt, at 300°. About 1·2 grams were isolated.

Found: C=46·2; H=5·4; N=15·8; Cl=26·6.

$C_{10}H_{11}ON_3,2HCl$ (262·1) requires C=45·8; H=5·0; N=16·0; Cl=27·0 per cent.

The solution of the hydrochloride was strongly acid to litmus. After treatment with nitrous acid, it gave a deep red coloration with sodium-β-naphthoxide. It gave no coloration with sodium diazobenzene-*p*-sulphonate in sodium carbonate solution. With sodium nitroprusside in presence of sodium hydroxide, a pale brown colour developed, which changed to green on acidification with acetic acid, and was discharged by excess of the reagent. Potassium permanganate in cold acid solution, and ammoniacal silver nitrate, were both reduced in the cold. The properties and composition of the compound indicate that it is correctly represented as 2-p-*aminophenyl*-5-*methyl*-4-*glyoxalone* (XVIII, p. 671).

The *benzylidene* derivative was prepared by treating 0·4 gram of the hydrochloride, dissolved in 8 c.c. of water, with 0·45 gram of sodium acetate and 0·4 gram of benzaldehyde. The oily, yellow product, which became crystalline on stirring, was collected and washed with water and with ether, leaving 0·4 gram of material. This decomposed on boiling with water, and dissolved only sparingly in alcohol and ethyl acetate. It was dried at 60° in a vacuum for analysis, and then melted at 156° (corr.), softening above 153°. The figures obtained indicated that it was the *acetate* of the *monobenzylidene* derivative.

Found: C=68·0; H=5·5; N=12·7.

$C_{17}H_{15}ON_3,C_2H_4O_2$ (337·3) requires C=67·6; H=5·7; N=12·5 per cent.

The mother liquors from the separation of the hydrochloride yielded small quantities of ammonia and aniline on suitable treatment.

Condensation of Acetaldehyde with Phenylcarbamide.

This condensation has been carried out using various conditions. For example, the phenylcarbamide was added slowly, with stirring, to a large excess of freshly distilled aldehyde, or was suspended in alcohol and mixed with aldehyde or acetal in various proportions. In every case the same product was obtained—two molecules of the phenylcarbamide uniting with one of the aldehyde to form *ethylidenebisphenylcarbamide*. This substance is practically insoluble in water, ether, ethyl acetate, or benzene, and very sparingly soluble in alcohol, from which it separates as a felted mass of silky needles melting at 220° (corr.).

Found: C = 64·4; H = 6·4; N = 18·8, 18·9.

$C_{16}H_{18}O_2N_4$ (298·3) requires C = 64·4; H = 6·2; N = 18·8 per cent.

Attempts to obtain partial hydrolysis and subsequent ring closure were unsuccessful.

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