SOME DERIVATIVES OF BENZIDINE.

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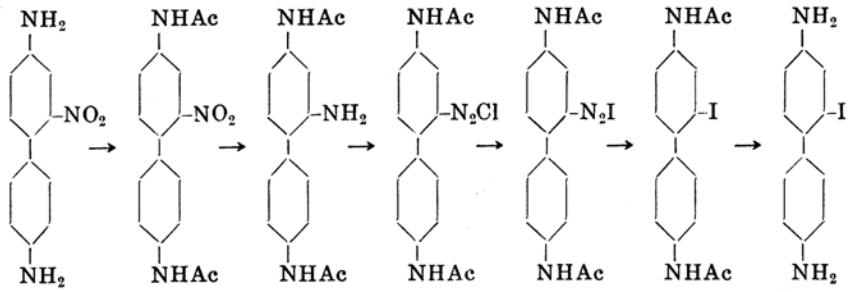
In connection with another work it became necessary to prepare 2-iodobenzidine (VII). Starting from 2-nitrobenzidine which could easily be produced by Täuber's method[1] the substance (VII) was obtained by the following series of processes :



As is to be expected, the difficulty encountered in this series of reactions arose from the ease with which the acetamido-groups were hydrolysed by the action of acids. On this account, the reduction of the nitro-compound (II) had to be carried out with a solution of stannous chloride and dry hydrogen chloride in glacial acetic acid. Similarly, in the production of the iodo-compound (VI) from the diazonium iodide (V), which was deposited in a stable crystalline form at ordinary temperature, the decomposition of (V) must not be effected in the usual way, that is, by heating in the presence of water. Fortunately, this difficulty could be got over by treating the solid diazonium iodide (V) with glacial acetic acid, when the decomposition took place even in the cold giving rise to the iodo-compound (VI) in an excellent yield.

It has been found that 2-nitrobenzidine exists in two forms, one recorded by Täuber having m.p. 143°C. and the other described in this paper m.p. 117°C. The detailed account of this discovery will be given in the experimental part, but a fact which deserves mention was that, although the author at first could prepare the lower melting form only, as

(1) *Ber.*, **23** (1890), 796.

soon as the higher melting form had once been produced, it was then the turn of the labile form which could no longer be obtained, a phenomenon which recalls the similar case in Liebermann's iso-cinnamic acid (m.p. 58°C.) which, when more stable allo-cinnamic acid (m.p. 68°C.) had been obtained, could be produced no more in his laboratory.[2]

It was found that 2-aminobenzidine obtainable by the reduction of 2-nitrobenzidine (I) also exhibits dimorphism, the melting point, 134°C. described by Täuber being that of the more stable form. As in the case of 2-nitrobenzidine, the less stable form having m.p. 50°C. was the first to be obtained, its conversion into the more stable form being easily accomplished. Unlike 2-nitrobenzidine, the labile form could be obtained even after the stable form had been produced.

Experimental.

2-Nitrobenzidine (I). The more stable form of this compound was obtained by the action of ammonia on the 2-nitrobenzidine sulphate which was produced by treating a solution of the benzidine sulphate in concentrated sulphuric acid with potassium nitrate.[1] Later Le Fèvre and Turner[3] found that in the nitration of benzidine the same result could be obtained by the use of the free base in place of the sulphate. The less stable form, the production of which was not observed by these workers, was found to be deposited when, for instance, a solution of the 2-nitrobenzidine sulphate (3.0 gr.) in boiling water (600 c.c.) was treated with a 20 per cent. ammonium hydroxide solution (7 c.c.). Some time after the addition of ammonia, the free base separated as an oil which, on being scratched, formed deep red, long needles which to the author's surprise melted, not at 143°C. as described by Täuber, but sharply at 117°C. As a matter of course, many attempts to prepare the higher melting form were made, which however let to no purpose for about a fortnight. Meanwhile, it was discovered that a slight but perceptible discoloration occurred in some of the crystals which had been put in a desiccator for some days. On examination, these crystals were found to melt at 143°C., showing that the conversion of the lower melting form into the higher had taken place. As to the remarkable phenomenon that the labile form was incapable of existence after the production of the stable form, it has already been stated in the introduction. Although both forms resembled chromic acid both in colour and in the crystalline form, there were still distinguishable difference

(2) *Ber.*, **23** (1890), 141, 2510.
(3) *J. Chem. Soc.*, **1926**, 1762.

between their appearances, the needles of the labile form being longer and having deeper colour than those of the more stable form. Both forms gave the same diacetyl compound.

2-Aminobenzidine. This compound was obtained by Täuber[1] by the reduction of 2-nitrobenzidine (I) with tin and hydrochloric acid. The author employed stannous chloride in place of tin. After the removal of tin from the reaction mixture by the use of hydrogen sulphide, the filtrate was greatly concentrated, when the trihydrochloride separated in transparent crystals. It was purified by treating with animal charcoal and the salt precipitated by the addition of concentrated hydrochloric acid to the concentrated filtrate.

As stated in the introduction, 2-aminobenzidine exists in two forms, one having m.p. 134°C. and the other 50°C. The former was obtained by Täuber.[1] The latter was produced as follows: when conc. ammonia (25 c.c.; D = 0.89) was added to a solution of the trihydrochloride (1.0 gr.) in water (15 c.c.) no precipitation occurred, but upon filtering the solution long needles separated after a short time, which melted at 50°C. A more concentrated solution of the salt than that employed above, on treatment with ammonia immediatly deposited the base as an oil which crystallized only after being left for a long time. At first, attempts to obtain the more stable form was not successful, the labile form remaining unchanged even on being heated above its melting point. But this change could be effected afterwards by the same treatment.

2-Amino-NN′-diacetylbenzidine (III). 2-Nitrodiacetyl benzidine (II), from which 2-aminodiacetyl benzidine (III) was obtained, was prepared by a modification of the method of Le Févre and Turner[3]: a solution of 2-nitrobenzidine (30 gr.) in glacial acetic acid (90 c.c.) was treated with acetic anhydride (30 c.c.). A short time later, the diacetyl compound commenced to separate. After heating the mixture on the water bath for an hour it was allowed to cool and the product collected and washed with acetic acid. The yield was 41.0 gr. (quantitative). Treatments such as described by Le Févre and Turner, that is, the addition of water to the reaction mixture before the filtration of the product and also the extraction of the product with methylated spirit are not necessary. 2-Nitrodiacetylbenzidine thus obtained melted, with darking and previous sintering, at 317°C.

Attempted reduction of 2-nitrodiacetyl benzidine for the preparation of the 2-aminodiacetyl benzidine with iron and acetic acid or with aluminium amalgam and aqueous alcohol failed. The reduction was, however, successfully accomplished as follows: 2-nitro-NN′-diacetylbenzidine (50.0 gr.) was added with constant shaking to a cold solution which was prepared by

saturating dry hydrogen chloride in a mixture of stannous chloride (130.0 gr.) and glacial acetic acid (600 c.c.). The nitro-compound gradually disappeared with a rise of temperature up to 50–60°C. The reduction product began to separate after half an hour or so from the start, when there still remained some original substance unattacked. It was necessary for the complete disappearance of the nitro-compound to shake the mixture for two hours during which hydrogen chloride was led in all the time. After that, the mixture was heated in a water bath at 40°C. for an hour and left over night. The double chloride thus separated was dried over soda lime under diminished pressure. The yield was 97.5 gr.

The powdered double salt (15.0 gr.) obtained above was added in small portions to 2000 c.c. of cold water with efficient agitation which was continued until the substance had completely dissolved (In mixing these two substances the above order should not be reversed, as, if water is added to the double chloride, it is apt to cake together, making its dissolution more difficult. Further, the dissolution must not be effected by heating, as this may cause the hydrolysis of the acetamido-groups). The disappearance of the original substance was followed by the separation of a white precipitate, probably a basic salt of tin, which increased in amount when hydrogen sulphide was passed into the mixture. All of tin present was thus precipitated mostly as the white precipitate and partly as the yellow sulphide. The clear filtrate separated from the precipitates, on treatment with a solution of crystalline sodium acetate (25.0 gr.), quickly deposited 2-aminodiacetyl benzidine (III) as white powder which was filtered after a time. The yield was over 80% of the theoretical, calculated on the 2-nitrodiacetyl benzidine employed. The 2-aminodiacetyl benzidine thus obtained was pure enough for further experiment as indicated by its melting point (260–262°C.). For purification, 0.24 gr. of the substance was dissolved in about 600 c.c. of boiling water and the solution concentrated until its bulk reached 200 c.c. On cooling, light, lustrous crystals (0.23 gr.) melting at 261–262°C. was obtained (Found : N = 15.1%. $C_{16}H_{17}O_2N_2$ requires N = 14.8%).

2-Iodo-NN'-diacetylbenzidine (VI). An ice cold, 15 per cent. hydrochloric acid solution (90 c.c.) was well mixed with powdered 2-aminodiacetyl benzidine (15.0 gr.). The pasty mass thus obtained after the addition of cold water (40 c.c.), was treated, with cooling by ice, with powdered sodium nitrite (3.8 gr.) in small portions at a time with mechanical agitation. After half an hour, a solution of potassium iodide (10.5 gr.) was added to the reaction mixture, when the diazonium iodide (V) separated as a brownish-red precipitate which did not decompose unless heated at a fairly high temperature. As however it was found that the heating of diazonium iodide

suspended in the reaction mixture caused at the same time the hydrolysis of the acetamido-groups, it was filtered off after 30 minutes from the addition of potassium iodide, pressed and without washing with water (for it is more or less soluble in fresh water.), added to cold glacial acetic acid (200 c.c.). The decomposition set in at once with copious evolution of gas, 2-iododiacetyl bezidine separating as a yellow precipitate which was collected and washed with acetic acid. The dried crude product, 16.1 gr., was redissolved in boiling acetic acid (1000 c.c.) and treated with animal charcoal. The clear filtrate was concentrated until the liquid had one-third the original bulk, when the crystals began to appear. Yellow short needles thus obtained (13.4 gr.) had m.p. 310–311°C. (Found : N = 7.4%. $C_{16}H_{15}O_2N_2I$ requires N = 7.1%).

Dihydrochloride of 2-Iodobenzidine. A suspension of 2-iododiacetyl benzidine (10.0 gr.) in conc. HCl (25 c.c.) and ethyl alcohol (100 c.c.) was heated under reflux on the water bath for two hours with occasional shaking. The disappearance of the original substance for which one hour's heating was necessary was followed by the gradual separation of the dihydrochloride of 2-iodobenzidine in small needles. After requisite time, it was cooled and the reddish yellow crystals collected and washed with ethyl alcohol. The yield was 9.3 gr. (Found : HCl = 18.7 ; N = 7.3%. $C_{13}H_{11}N_2I \cdot 2HCl$ requires HCl = 19.0 ; N = 7.3%).

Sulphate of 2-Iodobenzidine. 2-Iododiacetyl benzidine (3.1 gr.) suspended in ethyl alcohol (30 c.c.), conc. H_2SO_4 (3 c.c.), and water (9 c.c.) was heated at 100°C. for 5 hours. Most of the original substance disappeared in two hours. A small trace of the insoluble matter was removed by means of hot filter. The filtrate, on being left over night, gave 2.7 gr. of the crystalline sulphate of 2-iodobenzidine (Found : H_2SO_4 = 23.6%. $C_{12}H_{11}N_2I \cdot H_2SO_4$ requires H_2SO_4 = 24.0%).

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