CCCXI.—*Orientation Effects in the Diphenyl Series. Part IV. The Reduction of Bandrowski's and of Strakosch's Dinitrobenzidines, and the Condensation of the Products with Benzil. The Nitration of 2-Nitrodiacetylbenzidine and of 4 : 4′-Dibromodiphenyl.*

By RAYMOND JAMES WOOD LE FÈVRE, DANIEL DONALD MOIR, and EUSTACE EBENEZER TURNER.

IT was recently shown (Le Fèvre and Turner, J., 1926, 1759) that Cain's supposed 3 : 3′-dinitrobenzidine (Bandrowski's dinitrobenzidine) was the 2 : 3′-derivative, but, as was then fully realised, one difficulty still remained in connexion with the supposed identity of the two quinoxalines obtained by Cain and later by Brady and McHugh (J., 1923, **123**, 2047) by condensation with benzil of the tetra-amines derived from Bandrowski's and Strakosch's dinitrobenzidines. In view of the difficulty of purifying Bandrowski's compound (compare Le Fèvre and Turner, *loc. cit.*), an obvious explanation of the above facts was that the quinoxaline obtained from the Bandrowski material actually was derived from the Strakosch product, present as an impurity in the specimens of Bandrowski's dinitrobenzidine used for reduction.

We hesitated to advance this as a solution of the problem in the light of the conclusions of Brady and McHugh, but, in view of the fact that the Bandrowski's dinitrobenzidine prepared by Le Fèvre and Turner (*loc. cit.*) had m. p. 236—237°, *i.e.*, higher than that given by previous workers, we have carefully re-investigated the compounds concerned. We find that, in spite of the difficulties mentioned above, Bandrowski's dinitrobenzidine, *melting at* 233°, does, on reduction, followed by treatment with benzil in glacial acetic acid, give, as the most readily isolable product, a quinoxaline which is undoubtedly identical with that derived normally from 3 : 3′ : 4 : 4′-tetra-aminodiphenyl, and that therefore the initial Bandrowski's dinitrobenzidine must have contained some 3 : 3′-dinitrobenzidine.

There is a very marked difference in the behaviour of the two tetra-amines when treated with benzil. With that derived from Strakosch's dinitrobenzidine, a copious precipitate is obtained, but with that derived from Bandrowski's dinitrobenzidine (m. p. 233°, or a little lower), only a *small quantity* of precipitate results. The smallness of the yield was not mentioned by previous authors, and the foregoing explanation was therefore not suspected. The amount of Strakosch's dinitrobenzidine necessary to depress the m. p. of pure Bandrowski's dinitrobenzidine from 236—237° to 233° has been estimated, by examining artificial mixtures, as 2—3%. Such a proportion is in approximate agreement with the yields of quinoxaline obtained from various samples (see Experimental).

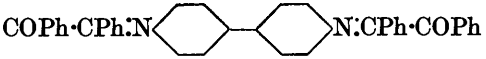
During the progress of this work, Hodgson (J., 1926, 2384) showed that some 3 : 3′-dinitrobenzidine was *formed* during the nitration of diphthalylbenzidine, but he did not attempt to demonstrate the presence of the 3 : 3′-isomeride in what has always been called Bandrowski's dinitrobenzidine, *i.e.*, a compound melting in the neighbourhood of 233°.

Methods previously described (Brunner and Witt, *Ber.*, 1887, **20**, 1024; Brady and McHugh, *loc. cit.*) for the reduction of Bandrowski's dinitrobenzidine proved unsatisfactory, but it was readily effected by iron powder, water, and ferric chloride.

Brady and McHugh showed that the two tetra-amines behaved very differently towards nitrous acid. A marked contrast was also observed when each was warmed in dilute acetic acid solution with acetic anhydride. In one case (2 : 3′ : 4 : 4′), bunches of white needles slowly separated from a purple solution, whilst in the other case there was immediate formation of an iridescent cream-coloured paste of minute needles. The compounds formed were the expected *tetra-acetyl* derivatives.

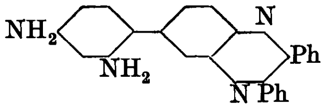
It was shown (Le Fèvre and Turner, J., 1926, 2476) that Cain's benzidine–benzil condensation product was dibenzoylbenzylidenebenzidine (I). 2 : 3′ : 4 : 4′-Tetra-aminodiphenyl (Bandrowski's tetra-amine) would therefore be expected to condense rapidly with

(I.)



benzil in cold glacial acetic acid solution to give (II), which should condense further with benzil only at higher temperatures. We

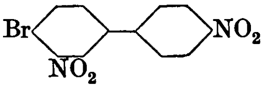
(II.)

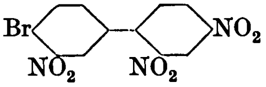


find that (II) is soluble in cold acetic acid, and that on heating the solution in which it is formed it undergoes further condensation with production of what is evidently a mixture of the two benzoylbenzylidene derivatives and the dibenzoylbenzylidene derivative corresponding with (I).

Although we have improved upon the usual process for obtaining Bandrowski's dinitrobenzidine, we attempted to prepare the corresponding tetra-amine without recourse to the parent dinitrobenzidine. 4-Bromo-4′-nitrodiphenyl was nitrated to give 4-*bromo-3 : 4′-dinitrodiphenyl* (III) which on further nitration gave 4-bromo-2′ : 3 : 4′-trinitrodiphenyl (IV) (Le Fèvre and Turner, J., 1926, 2041). Small quantities of the latter compound were readily convertible into 2′ : 3 : 4′-*trinitro*-4-*aminodiphenyl*, but the large-scale conversion proved unsatisfactory. The reduction of the trinitroamine was accordingly not fully investigated.

(III.)



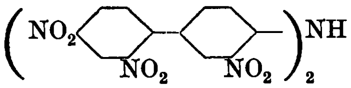


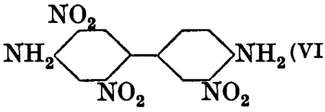
(IV.)

When (IV) was dissolved in boiling nitrobenzene, and dry ammonia was passed through, a bright yellow substance was obtained, apparently 4 : 4′-*bis*-op-*dinitrophenyl*-2 : 2′-*dinitrodiphenylamine* (V). The results of similarly treating other compounds containing reactive halogen atoms are recorded in the experimental part.

When attempting to prepare 2 : 3′-dinitrobenzidine from 2-nitrodiacetylbenzidine (Le Fèvre and Turner, *loc. cit.*), we observed that an impure product occasionally results, apparently owing to over-nitration. We have now obtained from such products, by application of the method used for preparing Bandrowski's dinitrobenzidine from diphthalylbenzidine, the sparingly soluble *sulphate* of 2 : 5 : 3′-*trinitrobenzidine* (VI), the constitution of which is proved

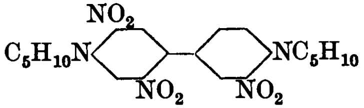
(V.)



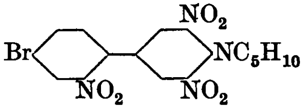


(VI.)

by its conversion by the perbromide method into 4 : 4′-*dibromo-2 : 5 : 3′-trinitrodiphenyl*, this in turn being identified by its ready conversion into a *di*piperidino-compound, *viz.*, 2 : 5 : 3′-*trinitro-4 : 4′-dipiperidinodiphenyl* (VII).



(VII.)



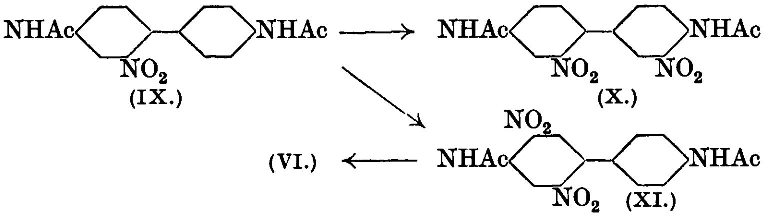
(VIII.)

Lellmann (*Ber.*, 1882, **15**, 2838) had previously isolated by over-nitration of dibromodiphenyl a trinitro-derivative, having a m. p.

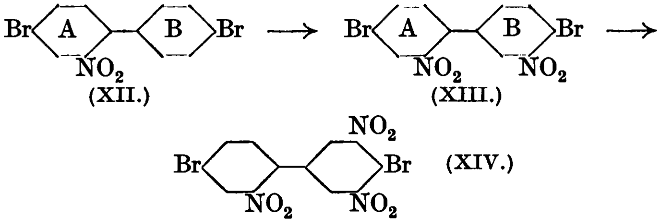
some 70° lower than that of the above compound. Lellmann's compound is, however, the isomeric 4 : 4′-*dibromo*-2 : 3′ : 5′-*trinitrodiphenyl* (XIV), since 4-*bromo*-2 : 3′ : 5′-*trinitro*-4′-*piperidinodiphenyl* (VIII) is formed from it with great readiness.

Comparison of the results now obtained with those previously recorded (this series) appears to show that, amongst the examples studied, the *op*- directive influence of groups decreases in the order NHAc > *p*-NHAc·C_6H_4 > *p*-Br·C_6H_4 > Br, the first being very powerful. In the light of this, it is possible to discuss the complete nitration of 2-nitrodiacetylbenzidine (IX) and of 4 : 4′-dibromo-2-nitrodiphenyl.

The former is now known to give as the main product 2 : 3′-dinitrodiacetylbenzidine (X), but since it has been shown (Bell and Kenyon, J., 1926, 2705) that 4-acetamidodiphenyl nitrates in position 3, *i.e.*, in the nucleus containing the acetamido-group, it would not be surprising, particularly in view of the now established powerful directive effect of this group, if some of the isomeric 2 : 5-compound (XI) were also formed. Further nitration of a mixture of (X) and (XI) would only be expected to affect (XI). We have actually found that (X) is unaffected by fuming nitric acid at 25°, *i.e.*, under conditions more drastic than those under which the trinitro-compound (VI) was originally formed. The nitration of 2-nitrodiacetylbenzidine, therefore, in all probability proceeds in accordance with the scheme outlined above.



The nitration of 4 : 4′-dibromo-2-nitrodiphenyl has previously been shown (Dennett and Turner, J., 1926, 476) to be controlled entirely by the bromine atom in the ring B (XII), since nucleus A is rendered ineffective owing to the presence of the nitro-group : 4 : 4′-dibromo-2 : 3′-dinitrodiphenyl is therefore quantitatively produced. In the further nitration of this compound, each nucleus will be as ineffective upon the other as was A in (XII); that is, entry of the third nitro-group will be controlled only by the nitro-group and bromine atom present in the nucleus attacked. In nucleus B (XIII) these groups will both favour nitration in position 5, whilst in A (XIII) they have antagonistic influences. Nitration therefore occurs in B, with formation of the above 4 : 4′-dibromo-2 : 3′ : 5′-trinitrodiphenyl (XIV).


(XII.) (XIII.) (XIV.)

EXPERIMENTAL.

Preparation of 2 : 3′-*Dinitrobenzidine.*—The following modification of the usual process is more satisfactory, particularly as regards yield : Powdered diphthalylbenzidine (270 g.) was slowly dissolved in 1800 c.c. of fuming nitric acid (*d* 1·5), the temperature not being allowed to rise above 10°. After 15 minutes, the mixture was poured on 5 kg. of crushed ice, the resulting light yellow precipitate being washed first with boiling water and then with hot methylated spirit (yield, 350 g.).

For hydrolysis, 270 g. of the above product, previously dried at 100°, were dissolved in 1200 c.c. of concentrated sulphuric acid, and the solution was heated at 135—140° for 20 minutes. After being cooled, the acid solution was poured into 5 l. of water, the temperature not being controlled. The precipitate first formed redissolved as the temperature rose, and the nearly clear solution, after filtration, deposited long, yellow-brown needles when cooled. These were collected and crystallised from dilute sulphuric acid (1 : 4 by vol.). The crystals so obtained were ground with aqueous ammonia, and the red base (m. p. 225°) was filtered off. One crystallisation from phenol–alcohol gave a definitely crystalline specimen, m. p. 233°. Two further crystallisations raised the m. p. to 234—235°, and to 236—237° (uncorr.), respectively, the final product being pure 2 : 3′-dinitrobenzidine.

Melting Points of Mixtures of 2 : 3′- *and* 3 : 3′-*Dinitrobenzidines.*—The specimens of the two bases used had m. p. 243—244° and 281—282° (corr.) respectively. A mixture containing 90% of 2 : 3′-base and 10% of 3 : 3′-base shrank at about 224°, showed definite signs of melting at 233°, and ran to a liquid at 237° ; one containing 94·8% of 2 : 3′- and 5·2% of 3 : 3′ base reached the same three stages respectively at 226°, 236°, and 238·6° ; and the 97·6–2·4% mixture at 238°, 239·9°, and 241·4°. The above figures were obtained by the use of a completely immersed, short-stem standard thermometer. The corresponding uncorrected figures, taken simultaneously with an ordinary thermometer, were: 218°, 227°, 231°; 220—221°, 229°, 232°; and 232°, 233°, 235°, respectively.

Reduction of Bandrowski's Dinitrobenzidine.—Preliminary experiments showed (1) that the tetra-amine is readily soluble in water, and (2) that the solution rapidly oxidises in the air. The following procedure was therefore adopted: 100 G. of iron powder were thoroughly wetted with 100 c.c. of water at 100°; 10 g. of 2 : 3′-dinitrobenzidine were then added, and the whole was well mixed. On the addition of a little ferric chloride, reduction proceeded vigorously, and was completed by ½ hour's heating with continuous stirring. Water was added, and the tetra-amine obtained in clear aqueous solution by filtration. Evaporation of this in a current of carbon dioxide (*a*) gave 2 : 3′ : 4 : 4′-tetra-aminodiphenyl as a purplish solid.

Reduction of Strakosch's Dinitrobenzidine.—10 G. of the dinitrobenzidine were shaken in a litre flask with 150 c.c. of methylated spirit until in fine suspension. 200 C.c. of water were added, followed by 70 g. of sodium hyposulphite, and the mixture was heated on the boiling water-bath for an hour. During this time, the colour changed from red to pale grey, and the suspended solid almost completely dissolved. The alcohol was then distilled off, the residue extracted with a mixture of water (150 c.c.) and concentrated hydrochloric acid (150 c.c.), the extract filtered, and the filtrate evaporated to about 2/3 of its original bulk. On cooling, pale brown needles of 3 : 3′ : 4 : 4′-tetra-aminodiphenyl hydrochloride separated. These, after being crystallised from dilute hydrochloric acid, were ground with aqueous ammonia; the liberated base crystallised from a mixture of phenol and alcohol in greyish plates, m. p. about 172—173° (Found: N, 26·5, 26·3. Calc.: N, 26·2%).

Condensation of 2 : 3′ : 4 : 4′-*Tetra-aminodiphenyl with Benzil.*—(a) *In the cold.* The flask in which the evaporation and extraction (*a* above) had been effected was tared, after its contents had been dried, and the soluble material was extracted four times with 10 c.c. of warm glacial acetic acid. Filtration from a considerable quantity of dark-coloured insoluble material enabled the amount of tetra-amine in solution to be calculated (generally of the order of 2 g.). A solution of the required quantity of benzil in cold glacial acetic acid was added to the cooled filtrate. After some minutes, crystallisation could be induced by scratching, but even after 12 hours the amount of greenish-yellow precipitate was quite small. Reduction of 10 g. lots of specimens of Bandrowski's dinitrobenzidine, melting at 225—226°, 233°, and 237° (uncorr.), gave 1·9, 1·1, and 0·0 g. of "quinoxaline" respectively. The crystals appeared as radiating bunches of needles when examined under the microscope, and melted in the crude state at 292—300°. The product crystallised readily from salicylaldehyde (originally used as a reagent to detect a free amino-group) in long, thin, straw-coloured plates, m. p. 308—309° (uncorr.). Admixture with an authentic specimen of Strakosch's quinoxaline did not depress this m.p. (Cain, Coulthard, and Micklethwait, *loc. cit.*; Brady and McHugh, *loc. cit.*) (Found : N, 10·7. Calc. : 10·0%). The mother-liquors from this crystallisation were dark coloured, indicating that the salicylaldehyde had reacted with the green impurities in the crude quinoxaline (see below).

(b) *At* 100°. In earlier experiments, condensation was attempted using excess of benzil in glacial acetic acid at 100°. In most cases, no precipitation occurred, even on scratching. Dilution with water produced a gummy deposit, from which dilute alcohol extracted a yellowish-green powder, soluble in glacial acetic acid, xylene, benzene, chloroform, and acetone, but obviously a mixture, with a m. p. range of about 30°.

A very marked reaction occurred when the product was heated with salicylaldehyde, water being eliminated.

Condensation of 3 : 3′ : 4 : 4′-*Tetra-aminodiphenyl with Benzil.*—To 1 g. of tetra-amine dissolved in 15 c.c. of glacial acetic acid was added a solution of 2 g. of benzil in 5 c.c. of the same solvent. A precipitate was formed suddenly, and this, when viewed under the microscope, appeared as stout needles. Alcohol was added, the solid filtered, re-heated with alcohol, and then dried at 100°. The cream-coloured powder (m. p. crude, 303—306°) separated from salicylaldehyde in straw-coloured plates, m. p. 308° (Found : N, 10·7%). It was very sparingly soluble in glacial acetic acid and acetone, more soluble in benzene, readily soluble in chloroform, and crystallised well from xylene in parallelograms, m. p. 308° (uncorr.), 313° (corr.).

Colour Reactions with Concentrated Sulphuric Acid.—The benzil condensation products derived both from Bandrowski's and from Strakosch's tetra-amines gave nearly identical purplish-red colorations with concentrated sulphuric acid. The colour is clearly due to the quinoxaline structure, and not to the possible presence of benzoylbenzylidene groupings, since αβ-diphenylquinoxaline gave a reddish-orange colour, whilst dibenzoylbenzylidenebenzidine merely dissolved to a normal yellow solution, which after a few minutes set to a white mass of benzidine sulphate. The other colours disappear on the addition of water or on exposure to the air (compare Brunner and Witt, *loc. cit.*).

Preparation of 4-*Bromo*-2′ : 3 : 4′-*trinitrodiphenyl.*—The following method proved more satisfactory than that used in Part III of this series, as it avoided numerous wasteful crystallisations : An intimate mixture of 100 g. of 4-bromo-4′-nitrodiphenyl and 52 g. of potassium nitrate was slowly added to 300 c.c. of concentrated sulphuric acid at 70—80°. The resulting solution was heated at 90° for ¼ hour, then cooled and poured into water. Crystallisation of the resulting precipitate from glacial acetic acid gave 4-*bromo*-3 : 4′-*dinitrodiphenyl* as dull white needles, m. p. 135° (Found : Br, 24·8. $C_{12}H_7O_4N_2Br$ requires Br, 24·8%). A mixture of 8 g. of the latter with 4 g. of potassium nitrate was nitrated in 60 c.c. of concentrated sulphuric acid under the above conditions. The product melted at 176° after one crystallisation from glacial acetic acid.

2′ : 3 : 4′-*Trinitro*-4-*aminodiphenyl*.—4-Bromo-2′ : 3 : 4′-trinitrodiphenyl (3 g.) was heated with saturated alcoholic ammonia (15 c.c.) in a sealed tube at 150° for 8—10 hours. The product was filtered off, dried, and crystallised from glacial acetic acid. It formed yellowish-orange needles, m. p. 192—193° (Found : N, 18·7. $C_{12}H_8O_6N_4$ requires N, 18·4%). This procedure proving very tedious, the following modification was attempted : 20 G. of 4-bromo-2′ : 3 : 4′-trinitrodiphenyl were dissolved in 200 c.c. of boiling nitrobenzene, and a current of dry ammonia was passed through the solution for 2 hours. A yellow solid soon began to separate, and, after cooling, it was collected, washed with benzene, dried, and crystallised from phenol–alcohol, forming bright yellow needles, m. p. 256—257° (Found : N, 17·0. $C_{24}H_{13}O_{12}N_2$ requires N, 16·6%). The analysis and the fact that the substance separates unchanged after being heated with salicylaldehyde prove it to be 4 : 4′-*bis*-op-*dinitrophenyl*-2 : 2′-*dinitrodiphenylamine* (V). Its low solubility in solvents prevented a determination of its molecular weight.

Action of Ammonia upon Boiling Nitrobenzene Solutions of other Halogeno-nitro-compounds.—(*a*) Picryl chloride (10 g.) was dissolved in boiling nitrobenzene (50 c.c.), and ammonia passed in for 2 hours, although solid had begun to separate very soon. The mixture was cooled and the resulting solid was crystallised from glacial acetic acid and identified as trinitroaniline, m. p. 187—188°.

(*b*) 1-Chloro-2 : 4-dinitrobenzene (20 g.), treated similarly (50 c.c. of nitrobenzene), also gave a precipitate, which separated from glacial acetic acid, and had m. p. 180—182°. It was thus 2 : 4-dinitroaniline.

(*c*) 2 : 5-Dichloronitrobenzene (10 g.) dissolved in 25 c.c. of boiling nitrobenzene was apparently unaffected by ammonia.

(*d*) 4 : 4′-Dibromo-2 : 3′-dinitrodiphenyl was partially converted into the corresponding bromo-amino-compound under the above conditions.

Isolation of 2 : 5 : 3′-*Trinitrobenzidine*.—The crude hydrolysis product resulting from a nitration of 70 g. of 2-nitrodiacetylbenzidine was boiled with dilute sulphuric acid, the extract filtered, allowed to crystallise, and the resulting *sulphate* again crystallised from dilute sulphuric acid. It was ground with aqueous ammonia, and the liberated base crystallised three times from phenol–alcohol, dark red needles, m. p. 276°, being obtained (Found : N, 21·6. $C_{12}H_9O_6N_5$ requires N, 21·9%).

The *diacetyl* derivative was a yellow substance, m. p. above 300°.

4 : 4′-*Dibromo*-2 : 5 : 3′-*trinitrodiphenyl*.—A solution of trinitrobenzidine (3·2 g.) in 20 c.c. of concentrated sulphuric acid was diazotised in the usual manner by 1·4 g. of solid sodium nitrite. The solution was diluted by the addition of 100 g. of ice, and filtered; 3 c.c. of bromine dissolved in 12 c.c. of hydrobromic acid were added, and the oily *perbromide* which separated solidified after 15 minutes, and was filtered off. Decomposition by heating with 40 c.c. of glacial acetic acid proceeded smoothly, and gave rise to a cream-coloured, crystalline precipitate of 4 : 4′-*dibromo*-2 : 5 : 3′-*trinitrodiphenyl*, which separated from about 250 c.c. of glacial acetic acid in wads of needles, m. p. 251—252°. The substance reacted readily with piperidine to give the 4 : 4′-*dipiperidino*-compound, which crystallised from rectified spirit in matted needles, m. p. 160° (Found : N, 15·8. $C_{22}H_{25}O_6N_5$ requires N, 15·4%).

Nitration of 4 : 4′-*Dibromo*-2 : 3′-*dinitrodiphenyl*.—When a solution of this compound in nitric acid (*d* 1·5) was allowed to stand, according to Lellmann's instructions, it remained unaffected. 3 G. of the dinitro-compound in 30 c.c. of a mixture (1 : 5 by vol.) of concentrated sulphuric acid and nitric acid (*d* 1·5) were left for 20 hours. Water was then added, and the precipitate extracted with a large bulk of alcohol. The residue crystallised from toluene in colourless needles, m. p. 176—177°, and reacted very vigorously with piperidine, even in the cold, to give the orange-coloured 4-*bromo*-2 : 3′ : 5′-*trinitro*-4′-*piperidinodiphenyl*, which, after being crystallised from much glacial acetic acid, melted at 194° (Found : N, 12·5. $C_{17}H_{15}O_6N_4Br$ requires N, 12·4%).

3 : 4′-*Dinitro*-4-*anilinodiphenyl*.—This substance was obtained by heating 4-bromo-3 : 4′-dinitrodiphenyl with excess of aniline at the b. p. of the latter for 5 minutes. It separated from glacial acetic acid in orange leaflets, m. p. 155—156°.

3 : 2′ : 4′-*Trinitro*-4-*anilino- and* -4-*methylanilino-diphenyl*.—These were readily obtained by heating 4-bromo-3 : 2′ : 4′-trinitrodiphenyl with excess of aniline and methylaniline respectively. The *anilino*-derivative crystallises from glacial acetic acid in orange-red leaflets,

m. p. 190—191°, and the *methylanilino*-derivative from the same solvent in deep red leaflets, m. p. 212°.

Part of the expenses of this investigation were met by grants allocated to two of us by the Chemical Society, and one of us (R. J. W. Le F.) is indebted to the Advisory Committee of the Department of Scientific and Industrial Research for a maintenance grant

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[*Received, July 25th*, 1927.]