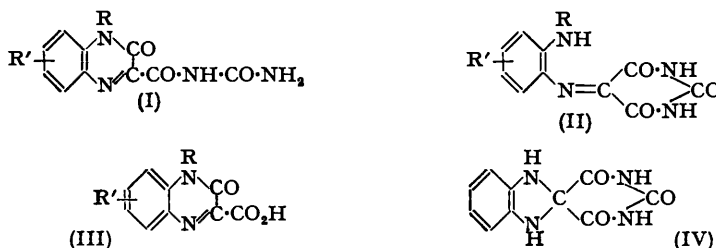


715. The Structure of the Product formed from Alloxan and *o*-Phenylenediamine in the Absence of Acid.

By R. B. BARLOW, H. R. ING, and I. M. LEWIS.

In the absence of acid, *o*-phenylenediamine and alloxan form a compound, $C_{10}H_8O_3N_4$, which must have one of three structures (I, II, and IV; $R = R' = H$). We have shown that (IV) cannot be correct and have re-assessed the merits of formulæ (I) and (II). Objections which have been thought to eliminate (I) are open to dispute. We have examined the ultra-violet absorption spectrum of the compound and compared it with those of the dihydroketoquinoxalinecarboxylic acid (III; $R = R' = H$) and the compound formed from 4 : 5-dichloro-2-dimethylaminoaniline and alloxan; we conclude that (I) is almost certainly the correct formula.

THE reactions of tolylenediamine and of *o*-phenylenediamine with alloxan in water were reported by Hinsberg (*Ber.*, 1885, 18, 1228; *Annalen*, 1896, 292, 247) to produce the dihydroketoquinoxalinecarboxyureides (I; $R = H$). When similar experiments were performed with *N*-mono-substituted *o*-phenylenediamines in methanol (Kühling, *Ber.*, 1893, 26, 540; Kühling and Kaselitz, *Ber.*, 1906, 39, 1314), in a mixture of ethanol, water, and acetic acid (Kuhn, Weygand, and Rudy, *Ber.*, 1935, 68, 633), and in pyridine (Tishler, Wellman, and Ladenburg, *J. Amer. Chem. Soc.*, 1945, 67, 2165), the products were formulated as the anils (II). All the compounds are easily hydrolysed to the dihydroketoquinoxalinecarboxylic acids (III) by alkali, and it is possible that they are actually all of the same type (Rudy and Cramer, *Ber.*, 1938, 71, 1234). A third type of structure, which does not appear to have been considered before, is the *spiro*-arrangement (IV); this was eliminated in the following way.

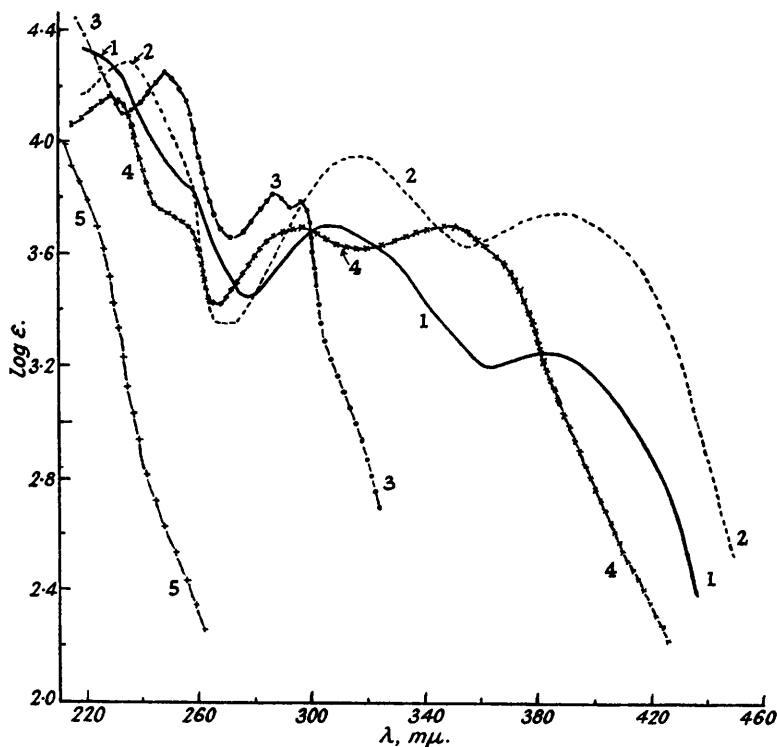


The product of the reaction between *o*-phenylenediamine and alloxan, which was the same whether the solvent was water or methanol, was reduced with hydrogen at room temperature and atmospheric pressure with Raney nickel catalyst suspended in methanol. The uptake of hydrogen corresponded to the addition of two hydrogen atoms, and the product was identical with that obtained from the reaction of *o*-phenylenediamine with dialuric acid in methanol. In addition to mixed m. p. tests, a check was provided by the ultra-violet absorption spectra, which were identical. This result rules out the *spiro*-structure (IV) and leaves only structures (I) and (II).

The compound (I or II; $R = R' = H$) has none of the properties associated with a free amino-group: (i) it is not basic and dissolves appreciably only in concentrated acid, from which it can be obtained unchanged by dilution with water; (ii) although Rudy and Cramer (*loc. cit.*) reported that it could be diazotized and coupled with 2-aminonaphthalene-3 : 6-disulphonic acid in strongly acid medium, we could not obtain an azo-dye when the substance was diazotized and treated with β -naphthol dissolved in alkali; (iii) it was recovered unchanged in 60% yield after it had been boiled under reflux with acetic anhydride for 6 hours.

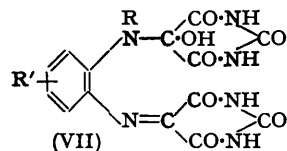
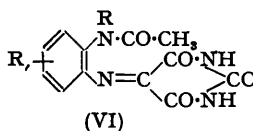
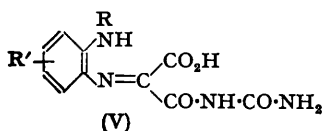
Against formula (I), on the other hand, must be set the observations reported by Kühling and Kaselitz (*loc. cit.*) that the compounds formed from their *N*-monosubstituted *o*-phenylenediamines and alloxan had the following properties: (i) when treated with very dilute alkali, they added a molecule of water, but very easily lost it again when dried in a desiccator; this was assumed to proceed *via* the open-ring compound (V); (ii) one of their compounds gave an acetyl derivative [postulated as (VI)]; (iii) another of their compounds could be converted by the action of hot acid into a substance which contained an additional alloxan fragment and which they thought to have the structure (VII).

Finally, Rudy and Cramer (*loc. cit.*; *Ber.*, 1939, 72, 227, 728; *Österreich. Chem. Ztg.*, 1939, 42, 329) stated that all the compounds from alloxan and *o*-phenylenediamines (whether diprimary or primary-secondary) were similar to that which they obtained from *NN*-dimethyl-*o*-phenylenediamine and alloxan and which they naturally thought must have the anil formula. This statement is open to dispute. While it seems very likely that the compounds from diprimary and from primary-secondary *o*-diamines are similar in structure, Rudy and Cramer themselves pointed out that their compound from *NN*-dimethyl-*o*-phenylenediamine was more soluble



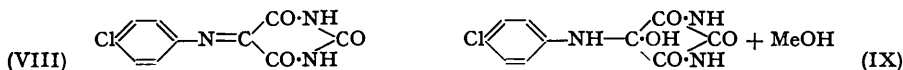
1. Compound from *o*-phenylenediamine and alloxan.
2. Reduced compound, identical with that obtained from *o*-phenylenediamine and dialuric acid.
3. Compound from 4 : 5-dichloro-2-dimethylaminoaniline and alloxan.
4. Dihydroketoquinoxalinecarboxylic acid.
5. Alloxan.

in acid, could form a hydrochloride, although this was unstable, and did not give a red colour in concentrated sulphuric as did the other compounds from alloxan and *o*-diamines.



For comparison we studied the action of alloxan on 4 : 5-dichloro-2-dimethylaminoaniline in hot acetic acid. As has already been briefly reported (Barlow, *J.*, 1951, 2226) analysis indicates the expected anil plus one molecule of water of constitution. In order to throw light on the structure of this compound, we examined the reaction of alloxan with *p*-chloroaniline. In acetic acid solution, these two formed a bright red compound, $\text{C}_{10}\text{H}_8\text{O}_3\text{N}_3\text{Cl}$, which was almost certainly the anil (VIII) since it was hydrolysed by dilute acid to *p*-chloroaniline; in methanol they produced a white substance which is very easily dehydrated (in an oven at 120°) to the anil (VIII) and appears to be the carbinol base plus methanol (IX). It seems unlikely that the product from 4 : 5-dichloro-2-dimethylaminoaniline and alloxan can have an anil or hydrated-anil structure because it is stable to the action of hot concentrated hydrochloric

acid. We tried to reach a positive conclusion about the formulæ of these compounds by a study of their catalytic hydrogenation but although both the compound from 4 : 5-dichloro-2-dimethylaminoaniline and the anil (VIII) could be reduced with hydrogen and Raney nickel at room temperature and atmospheric pressure, and the absorption corresponded to the addition



of two hydrogen atoms, we obtained a mixture of products in each reduction. The principal reduction product of the compound from 4 : 5-dichloro-2-dimethylaminoaniline was not identical with the compound formed from 4 : 5-dichloro-2-dimethylaminoaniline and dialuric acid; nor with hydrochloric acid did it give a salt identical with that obtained from monochlorobarbituric acid and the diamine. Similarly the principal reduction product of the anil (VIII) did not give with hydrochloric acid a salt identical with that formed from monochlorobarbituric acid and *p*-chloroaniline.

We measured the ultra-violet absorption spectra of the compounds in water, and it is clear that the substance formed from 4 : 5-dichloro-2-dimethylaminoaniline and alloxan does not absorb in at all the same way as the compound from *o*-phenylenediamine and alloxan (figure). If the former is an anil, then the latter is certainly not the anil (II; R = H). Further and more satisfactory evidence is obtained by comparing the absorption of the dihydroketoquinoxaline-carboxylic acid with that of the products from alloxan and *o*-phenylenediamine and from dialuric acid and *o*-phenylenediamine (figure). This leaves little doubt that Hinsberg's original formula is correct. We have not so far confirmed this by synthesis. Examination of the ultra-violet absorption spectra of the compounds obtained by Kühling and others from primary-secondary *o*-diamines should decide whether these too have the same structure (I).

EXPERIMENTAL.

Analyses are by Mr. J. M. L. Cameron and Miss R. H. Kennaway and by Drs. Weiler and Strauss. All m. p.s are uncorrected.

Preparation of the Compound.—When equimolar solutions of *o*-phenylenediamine and alloxan in methanol or water were mixed, a greenish-yellow crystalline porridge was formed within from a minute to a few seconds, depending on the temperature. This was recrystallized from acetic acid; it had m. p. 240° (decomp.) [Hinsberg (*loc. cit.*) recorded m. p. 250° (decomp.)] (Found: C, 51.9; H, 3.5; N, 23.6. Calc. for C₁₀H₈O₃N₄: C, 51.7; H, 3.45; N, 24.1%). The yield was almost theoretical. Ultra-violet light absorption in water: maxima at 305 and 385 mμ (ε = 4960 and 964, respectively); minima at 276 and 360 mμ (ε = 2790 and 914, respectively).

Reduction.—The compound (0.5 g.), suspended in methanol, was reduced with hydrogen and Raney nickel at room temperature and atmospheric pressure. The reduction was stopped after the absorption corresponded to the addition of two hydrogen atoms. The mixture was heated to dissolve the reduction product and filtered. The yellow powder (0.4 g.), which separated from the filtrate, was recrystallized from alcohol; the compound had m. p. 260° (Found: C, 51.7; H, 3.9; N, 23.9. C₁₀H₁₀O₃N₄ requires C, 51.3; H, 4.3; N, 23.9%). Ultra-violet light absorption in water: maxima at 234, 316, and 386 mμ (ε = 19,200, 8850, and 5560); minima at 219, 269, and 354 mμ (ε = 14,800, 2240, and 4180).

The same compound was also produced when equimolar solutions of *o*-phenylenediamine and dialuric acid in methanol were heated under reflux for 2 hours and then left to cool. The yellow needles so formed were recrystallized from ethanol and then had m. p. 260° (Found: C, 51.3; H, 4.4; N, 23.7%) (yield, 80%).

A mixture of this substance and the reduction product also melted at 260° and the ultra-violet absorption spectra of the two materials dissolved in water were identical.

The Compound from 4 : 5-Dichloro-2-dimethylaminoaniline and Alloxan.—The preparation of this has already been described (Barlow, *loc. cit.*). A specimen (Found: N, 15.8. Calc. for C₁₂H₁₂O₃N₄Cl₂: N, 16.2%) did not give a colour with concentrated sulphuric acid. Ultra-violet light absorption in water: maxima at 249, 286, and 296 mμ (ε = 17,900, 6600, and 6080); minima at 234, 272, and 292 mμ (ε = 12,600, 4590, and 5750).

The Compounds from 4 : 5-Dichloro-2-dimethylaminoaniline and Dialuric and Chlorobarbituric Acids.—Equimolar solutions of the diamine and dialuric acid in methanol were boiled under reflux for 2 hours. A yellow substance rapidly separated and was crystallized from a large volume of alcohol. The compound did not melt below 320° (Found: C, 41.2; H, 3.5; N, 17.3. C₁₂H₁₂O₃N₄Cl₂·H₂O requires C, 41.2; H, 3.4; N, 16.9%) (yield, 75%). In the same way, equimolar solutions of the diamine and monochlorobarbituric acid in alcohol were boiled under reflux for 1 hour. Orange-yellow crystals were formed when the solution had cooled. These were filtered off and recrystallized from methanol; the compound had m. p. 184° (Found: C, 39.4; H, 3.75; N, 15.2. C₁₂H₁₃O₃N₄Cl₂ requires C, 39.3; H, 3.5; N, 15.5%).

Model Experiments with p-Chloroaniline.—(i) Equimolar solutions of alloxan and *p*-chloroaniline in hot glacial acetic acid were mixed and left overnight. The solvent was distilled off under reduced pressure, and the red residue was extracted with ether in a Soxhlet apparatus. The red anil which

crystallized from the hot ether (m. p. 232°) was recrystallized from acetone by the addition of light petroleum (b. p. 40—60°); it then had m. p. 239° (decomp.) (Found: C, 47.6; H, 2.5; N, 16.7. $C_{10}H_4O_2N_3Cl$ requires C, 47.8; H, 2.4; N, 16.7%) (yield, 60—70%). The *anil* was very soluble in alcohols, acetone, and glacial acetic acid, less in ethyl acetate, slightly in ether and chloroform, very slightly in benzene, and not at all in light petroleum (b. p. 40—60°). When it was treated with 2*N*-hydrochloric acid in the cold, followed by 2*N*-sodium hydroxide until alkaline, *p*-chloroaniline (40%; m. p. 67—68°) was recovered. Beilstein and Kurbatow (*Annalen*, 1875, 176, 29) recorded m. p. 69—70°. No *p*-chloroaniline was isolated when the compound was treated directly with alkali.

(ii) Equimolar solutions of *p*-chloroaniline and alloxan in methanol were mixed and after a time varying from a day, if the solutions were at room temperature, to minutes, if they were hot, a white solid began to separate. The crude, slightly pink product was filtered from the red mother-liquor and left to dry in air. The yield almost theoretical. The *substance* was unstable in solution and formed deep red solutions in solvents such as alcohol or glacial acetic acid. It became red above 120° and finally decomposed, becoming black, at 238—239°. It was insoluble in water but crystallized from 50% aqueous methanol (Found: C, 43.6; H, 3.4; N, 14.1. $C_{11}H_{12}O_5N_3Cl$ requires C, 43.8; H, 4.0; N, 13.9. Loss in weight when dried at 110—120°, 16.5, 16.6. $C_{10}H_8O_3N_3Cl + CH_4O + H_2O$ requires 16.9%). The product of dehydration, m. p. 238—239° (decomp.), was identical with the *anil* formed in acetic acid. When shaken with cold dilute alkali the *substance* was rapidly converted into *p*-chloroaniline, m. p. 66—68°.

(iii) Equimolar solutions of monochlorobarbituric acid and *p*-chloroaniline in methanol were mixed; after a few seconds a precipitate formed. This was left overnight, then filtered off and recrystallized twice from 30% aqueous methanol; the *compound* had m. p. 217—218° (decomp.) (Found: C, 41.6; H, 3.2; N, 14.0. $C_{10}H_8O_3N_3Cl_2$ requires C, 41.4; H, 3.1; N, 14.5%). The yield was almost theoretical. The *substance* was converted into *p*-chloroaniline, m. p. 67—68°, by treatment with alkali.

The Dihydroketoquinoxalinecarboxylic Acid.—This was prepared from the compound $C_{10}H_8O_3N_4$ by the action of either cold 2*N*-sodium hydroxide overnight or boiling 4*N*-sodium hydroxide until no more ammonia was evolved (6 hours). The compound was precipitated with acid and recrystallized from ethanol; it had m. p. 260—261° (decomp.) (Found: C, 57.3; H, 3.4; N, 14.8. Calc. for $C_9H_6O_3N_4$: C, 56.9; H, 3.2; N, 14.7%). Hinsberg (*loc. cit.*) recorded m. p. 265°. Ultra-violet light absorption in water: maxima at 229, 297, and 347 $m\mu$ ($\epsilon = 14,100, 5030, \text{ and } 5000$); minima at 267 and 321 $m\mu$ ($\epsilon = 2630$ and 4180).

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