923. *Two Hypothetical Metabolites of Proguanil ("Paludrine").*

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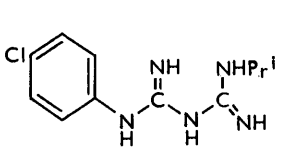
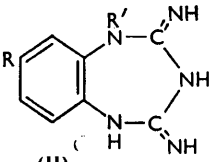
Several benzoxazoles and benz-epines, modelled on proguanil, have been prepared from the appropriate amines and dicyandiamides or dicyanimide respectively. None of the compounds showed any antimalarial activity.

The discovery [1] that proguanil ("Paludrine") (I) itself is not an antimalarial agent but that it is transformed *in vivo* into a highly active metabolite prompted speculation concerning the nature of the active material. The experiments here described were mostly carried out before the identification [2] of the metabolite as 4 : 6-diamino-1-*p*-chlorophenyl-1 : 2-dihydro-2 : 2-dimethyl-1 : 3 : 5-triazine.

Oxidative cyclisation of proguanil could give 5-chloro-2-N^3-*iso*propylguanidinobenziminazole, but this compound is inactive against *Plasmodium gallinaceum*.[3] An alternative cyclisation leads to the benzotriazepine (II; R = Cl, R′ = Pr^i). The unsubstituted derivative (II; R = R′ = H) had earlier [3] been obtained from *o*-phenylenediamine and dicyanimide. The 1-methyl derivative (II; R = H, R′ = Me) was formed under similar conditions from *N*-methyl-*o*-phenylenediamine and likewise did not react with aqueous nitrous acid. As the product from this reaction could have been 2-guanidino-1-methylbenziminazole, formed by reaction of one cyano-group of the dicyanimide with the diamine to give 2-cyanoamino-1-methylbenziminazole followed by addition of the ammonia produced to



(I)



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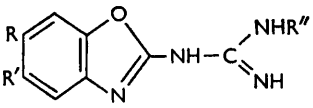

(III)

the second cyano-group, this compound was prepared from *N*-methyl-*o*-phenylenediamine and dicyandiamide; its monopicrate was different from the dipicrate obtained from the triazabenzepine (II; R = H, R′ = Me) under the same conditions. The chlorobenzotriazepines (II; R = Cl, R′ = H, Et, and Pr^i) were then synthesised from the appropriate diamines, obtained by the catalytic reduction of the corresponding nitro-amines and isolated as the picrates which were then converted into the sulphates. The normal course of a *P. gallinaceum* infection in chicks was not, however, altered by the benzotriazepine (II; R = R′ = H) or any of its substituted derivatives described here; we thank Miss A. Bishop and Mrs. A. M. Yates for this information.

Hydroxylation of sulphanilamide *ortho* to the amino-group in man and rabbits,[4] and of

[1] Hawking, *Nature*, 1947, **159**, 409.
[2] Crowther and Levi, *Brit. J. Pharmacol.*, 1953, **8**, 93, and earlier papers.
[3] Acheson, King, and Spensley, *Nature*, 1947, **160**, 53; *J.*, 1948, 1366.
[4] Williams, *Biochem. J.*, 1946, **40**, 219; 1947, **41**, 1.

orthanilamide in rabbits,[5] has been established. A similar substitution of proguanil followed by elimination of ammonia would lead to the benzoxazole (III; R = Cl, R′ = H, R″ = Pr^i) which was next synthesised. The unsubstituted benzoxazole [6] and two derivatives [7] had been obtained earlier from the *o*-aminophenols, hydrochloric acid, and dicyandiamide. This condensation was used for the synthesis of the benzoxazoles (III; R = R″ = H, R′ = OMe; R = Cl, R′ = R″ = H; and R = R′ = Cl, R″ = H). The 2-*N*^{3}-*iso*propylguanidinobenzoxazoles (III; R″ = Pr^i) were obtained similarly but were much more difficult to crystallise. Early attempts to isolate the benzoxazole (III; R = Cl, R′ = H, R″ = Pr^i) from the reaction mixture as the picrate, which was purified, gave only 2-amino-6-chlorobenzoxazole picrate, but once the crude base (III) had been obtained crystalline direct from the reaction mixture no further difficulty was encountered. Imperial Chemical Industries Limited, Dyestuffs Division, in 1953 kindly tested the benzoxazoles (III; R = R″ = H, R′ = OMe) against *P. berghei* and *P. gallinaceum*, and the compound (III; R = Cl, R′ = R″ = H) against *P. gallinaceum*, but they proved inactive. We have been informed that this is also the case with the hypothetical metabolite (III; R = Cl, R′ = H, R″ = Pr^i) of proguanil.

In our hands Roberts and Rhys's synthesis [8] of 2-amino-5-chlorophenol proved more satisfactory than that of Theilacker's.[9] 5-Chloro-2-nitrophenol could be obtained only in very small yield from 2 : 4-dichloronitrobenzene and sodium hydroxide under a variety of conditions. *m*-Chlorophenol was obtained crystalline for the first time and in improved yield by modifying a published method.[10] There appears to be no rigorous proof in the literature of the structure of 1 : 2-dichloro-4 : 5-dinitrobenzene. The nitro-groups must be *ortho* to each other as condensation with ribitylamine, reduction, and then condensation with alloxan afford a dichloro-9-ribityl*iso*alloxazine. The *iso*alloxazine is isomorphous with vitamin B_2.[11] This suggests strongly that the structure given to the chlorodinitrobenzene is correct and it is supported by some infrared absorption measurements. Williams [12] and Thompson [13] have shown that in a series of 1 : 2 : 3 : 4-tetrasubstituted benzene derivatives a pronounced absorption band at 12·12 μ is consistent with vibrations of the vicinal hydrogen atoms on the benzene rings; for 1 : 2 : 4 : 5-tetrasubstituted derivatives absorption is usually minimal here but takes place in the 11·36—11·62 μ region. 1 : 2-Dichloro-4 : 5-dinitro-, 1 : 2-dichloro-4-hydroxy-5-nitro-, and 1-amino-4 : 5-dichloro-2-hydroxybenzene described have minimum absorption in paraffin paste at *ca.* 12·1 μ, with maxima towards shorter and longer wavelengths, while 1 : 2-dichloro-4-nitrobenzene, examined for comparison, had a very strong absorption maxima at 12·11 μ.

Experimental

2 : 4-Diamino-1-methyl-1 : 3 : 5-benzotriazepine (II; R = H, R′ = Me).—*N*-Methyl-*o*-nitroaniline (2·02 g.) was hydrogenated over Raney nickel in methanol (20 ml.) to the diamine, filtered into concentrated hydrochloric acid (1·32 ml.), and added to sodium dicyanimide (1·17 g.) in water (5 ml.). Most of the methanol evaporated after boiling on a steam-bath for 1 hr., and the residual suspension of a black oil was treated with methanolic picric acid (6·0 g., 2·0 mol.). The *benzotriazepine dipicrate* (5·9 g., 68%) rapidly separated and crystallised from methanol (charcoal) in yellow needles, m. p. 216—217° (decomp.) (Found: C, 39·1; H, 2·8; N, 23·1. $C_9H_{11}N_5,2C_6H_3O_7N_3$ requires C, 38·9; H, 2·6; N, 23·8%). Decomposition of the dipicrate in hot 2-ethoxyethanol solution with alcoholic sulphuric acid gave the *sulphate*, precipitated by ether. After being washed with ether (to remove picric acid) this separated from aqueous ethanol in colourless needles, m. p. 252° (decomp., after softening at ~230°) (Found: C, 33·8; H, 5·8; N, 22·2; S, 9·5. $C_9H_{11}N_5,H_2SO_4,2H_2O$ requires C, 33·4; H, 5·3; N, 21·7; S, 9·9%).

The sulphate (0·2 g.), suspended in sulphuric acid (0·053 ml.; *d* 1·84) in water (2 ml.), was

[5] Stubbs and Williams, *Biochem. J.*, 1947, **41**, xlix.
[6] Smith, Kane, and Mason, *J. Amer. Chem. Soc.*, 1929, **51**, 2522.
[7] Nagano, Itoh, and Matsumura, *J. Amer. Chem. Soc.*, 1953, **75**, 2770.
[8] Roberts and Rhys., *J.*, 1937, 41.
[9] Theilacker, *Ber.*, 1938, **71**, 2065.
[10] Fieser and Thompson, *J. Amer. Chem. Soc.*, 1939, **61**, 382
[11] Kuhn, Weygand, and Moller, *Ber.*, 1943, **76**, 1044.
[12] Williams, *Rev. Sci. Instr.*, 1948, **19**, 135.
[13] Thompson, *J.*, 1948, 328.

treated with 10% aqueous sodium nitrite (0·86 ml.). No visible reaction took place in 2 hr. at room temperature and a sample gave no colour with alkaline β-naphthol. When heated to 90° the solid dissolved and after 1 hr. aqueous sodium picrate (0·32 g.) was added. The original benzepine dipicrate (0·28 g., 70%), m. p. and mixed m. p. 216—217° (decomp.), was precipitated.

2 : 4-*Diamino*-7-*chloro*-1 : 3 : 5-*benzotriazepine* (II; R = Cl, R′ = H).—The *benzotriazepine monopicrate* (4·05 g., 79%) was similarly prepared from 5-chloro-2-nitroaniline (2·02 g.), concentrated hydrochloric acid (1·17 ml.), sodium dicyanimide (1·04 g.), and picric acid (2·7 g.) and crystallised from methanol in short yellow needles, m. p. 263—264° (Found: C, 38·6; H, 2·5; Cl, 8·3. $C_8H_8N_5Cl,C_6H_3O_7N_3$ requires C, 38·3; H, 2·5; Cl, 8·1%). The *hemisulphate hemihydrate*, prepared from the picrate as above, separated from a large volume of water in colourless needles, m. p. 274° (decomp.) (Found: C, 36·0; H, 4·1; S, 6·0. $C_8H_8N_5Cl,\frac{1}{2}H_2SO_4,\frac{1}{2}H_2O$ requires C, 35·9; H, 3·7; S, 6·0%).

2 : 4-*Diamino*-8-*chloro*-1-*ethyl*-1 : 3 : 5-*benzotriazepine* (II; R = Cl, R′ = Et).—The *benzotriazepine dipicrate* (3·8 g., 58%) was similarly prepared from 5-chloro-*N*-ethyl-2-nitroaniline (1·90 g.), hydrochloric acid (0·95 ml.), sodium dicyanimide (0·85 g.), and picric acid (4·6 g.) and separated from aqueous methanol in irregular yellow prisms, m. p. 195—196° (decomp., with sintering at ~190°) (Found: C, 38·1; H, 2·9. $C_{10}H_{12}N_5Cl,2C_6H_3O_7N_3$ requires C, 37·8; H, 2·6%). The hydrated *sulphate*, obtained as before, separated from aqueous ethanol in colourless needles, m. p. 107—115° (with loss of solvent; after resolidification the colourless residue decomposed at ~170—180°) [Found: loss on drying at 100° *in vacuo*, 11·9; on dried material: S, 10·3. $C_{10}H_{12}N_5Cl,H_2SO_4,2\frac{1}{2}H_2O$ requires loss (to anhydrous material) 11·8; S (anhyd.) 9·5%].

2 : 4-*Diamino*-8-*chloro*-1-iso*propyl*-1 : 3 : 5-*benzotriazepine* (II; R = Cl, R′ = Pr^i).—The *benzotriazepine dipicrate* (17·2 g., 81%) was obtained as before from 5-chloro-2-nitro-*N*-*iso*propylaniline (6·4 g.), hydrochloric acid (3·0 ml.), sodium dicyanimide (2·66 g.), and picric acid (14·5 g.), and separated from ethanol as the solvate in thin yellow prisms, m. p. 208—210° (decomp. after sintering at ~180°) (Found: C, 39·7, 40·1; H, 3·4, 3·3; N, 20·0; Cl, 4·9. $C_{11}H_{14}N_5Cl,2C_6H_3O_7N_3,C_2H_5{\cdot}OH$ requires C, 39·7; H, 3·3; N, 20·4; Cl, 4·7%). Decomposition in 2-ethoxyethanol was unsatisfactory owing to the insolubility of the dipicrate, but its (11·7 g.) solution in hot *cyclo*hexanol (30 ml.) with concentrated sulphuric acid (6·0 ml.) in ethanol (20 ml.) followed by ether gave the *sulphate* (5·0 g., 86%) which was washed with ether and separated from aqueous ethanol in colourless plates, m. p. 175—177° (decomp.) (Found: C, 38·2; H, 4·6; S, 8·9. $C_{11}H_{14}N_5Cl,H_2SO_4$ requires C, 37·8; H, 4·6; S, 9·2%).

5-*Chloro*-N-*ethyl*-2-*nitroaniline*.—2 : 4-Dichloro-1-nitrobenzene (5·0 g.), ethylamine hydrochloride (4·3 g.), sodium hydroxide (2·1 g.), ethanol (10 ml.), and water (10 ml.) were slowly heated to 200° (5 hr.) in a sealed tube. The product was washed out with a little ethanol and diluted with water, and the amine collected. It separated from aqueous methanol in yellow prisms, m. p. 83° (4·2 g., 80%). This amine, prepared by other methods, is reported to have [14, 15] m. p. 83—84° and 75·5—76·5°.

5-*Chloro*-2-*nitro*-N-iso*propylaniline*.—2 : 4-Dichloro-1-nitrobenzene (8·4 g.), *iso*propylamine (5·2 g.), and ethanol (20 ml.) were heated at 200° for 6 hr. in a sealed tube. The *aniline* (8·3 g., 88%) was isolated as above, and separated from aqueous methanol (charcoal) in thin yellow needles, m. p. 50—51° (Found: C, 50·2; H, 5·5. $C_9H_{11}O_2N_2Cl$ requires C, 50·3; H, 5·1%).

2-*Guanidino*-1-*methylbenziminazole*.—*N*-Methyl-*o*-nitroaniline (4·0 g.) was hydrogenated to the diamine in ethanol (20 ml.) over Raney nickel and filtered into a mixture of concentrated hydrochloric acid (5·3 ml.), dicyandiamide (2·3 g.), and water (20 ml.). The mixture was refluxed (1 hr.) and methanolic picric acid (12·0 g., 2 mol.) added. The *benziminazole monopicrate* separated, and crystallised from ethanol (charcoal) in orange-yellow prisms, m. p. 193—195° (Found: C, 43·3; H, 3·3; N, 26·0. $C_9H_{11}N_5,C_6H_3O_7N_3$ requires C, 43·1; H, 3·3; N, 26·8%).

2-*Guanidino*-5-*methoxybenzoxazole* (III; R = R″ = H, R′ = OMe).—2-Amino-4-methoxyphenol (0·52 g.), ethanol (2 ml.), and hydrochloric acid (0·5 ml.; *d* 1·16) were heated to boiling, dicyandiamide (0·42 g.) added, and the whole heated under reflux for 2 hr. Water was added and the precipitate (0·7 g.) collected, dissolved in boiling water (30 ml.), and basified with aqueous sodium hydroxide. The *benzoxazole* was precipitated, and crystallisation from water gave colourless needles, m. p. 214° (0·4 g., 45%) (Found: C, 52·5; H, 4·9; N, 27·2. $C_9H_{10}O_2N_4$ requires C, 52·5; H, 5·0; N, 26·7%). The *picrate* separated from aqueous ethanol in the small yellow needles of the trihydrate, m. p. 220° (Found: C, 36·9; H, 4·2; N, 20·2. $C_9H_{10}O_2N_4,C_6H_3O_7N_3$ requires C, 36·8; H, 3·9; N, 20·1%).

[14] Laubenheimer, *Ber.*, 1878, **11**, 1156.
[15] Stoermer and Hoffmann, *Ber.*, 1898, **31**, 2533.

6-Chloro-2-guanidinobenzoxazole (III; R = Cl, R′ = R″ = H).—This was prepared similarly from 2-amino-5-chlorophenol (0·28 g.), ethanol (2 ml.), hydrochloric acid (0·2 ml.), and dicyandiamide (0·16 g.), and crystallisation from water (charcoal) gave small colourless needles of the *monohydrate*, m. p. 202° (Found: C, 42·3; H, 4·0; Cl, 15·4. $C_8H_7ON_4Cl,H_2O$ requires C, 42·1; H, 3·9; Cl, 15·5%). The base sublimed at 120° *in vacuo*, but lost most of its water when dried on a steam-bath (1 hr.) and then over phosphoric oxide (Found: C, 46·1; H, 3·6. $C_8H_7ON_4Cl$ requires C, 45·6; H, 3·3%). The *picrate* separated from water in small yellow needles, m. p. 265° (decomp.) (Found: N, 21·3. $C_8H_7ON_4Cl,C_6H_3O_7N_3$ requires N, 21·5%).

5 : 6-Dichloro-2-guanidinobenzoxazole (III; R = R′ = Cl, R″ = H).—This was similarly prepared from 2-amino-4 : 5-dichlorophenol (0·54 g.), water (5 ml.), hydrochloric acid (0·5 ml.), and dicyandiamide (0·42 g.). A precipitate was formed after 15 minutes' refluxing, which was then continued only for a further 30 min. The *benzoxazole*, isolated as before, separated from aqueous ethanol in colourless needles (0·3 g.), m. p. 250° (Found: C, 39·4; H, 2·5. $C_8H_6ON_4Cl_2$ requires C, 39·2; H, 2·5%).

2-N^3-iso*Propylguanidinobenzoxazole* (III; R = R′ = H, R″ = Pr^i).—2-Aminophenol (0·5 g.), water (2 ml.), and hydrochloric acid (0·5 ml.) were heated to boiling and *iso*propyldicyandiamide (0·52 g.) added. After refluxing (2 hr.) the mixture was cooled and basified and the aqueous layer decanted. The residual gum was warmed with water (10 ml.) and hydrochloric acid (0·5 ml.) until it dissolved. The *benzoxazole hydrochloride* (0·3 g.) was precipitated on cooling and separated from water, containing a trace of hydrochloric acid, in small colourless needles, m. p. 100° (Found: C, 45·7; H, 6·6; Cl, 13·6. $C_{11}H_{15}ON_4Cl,2H_2O$ requires C, 45·4; H, 6·5; Cl, 13·3%). The free *base*, obtained with aqueous alkali, separated from aqueous ethanol in prisms, m. p. 171° (Found: C, 60·9; H, 6·4. $C_{11}H_{14}ON_4$ requires C, 60·5; H, 6·4%). The *picrate*, yellow needles from 50% aqueous ethanol, had m. p. 202° (Found: C, 45·7; H, 3·8; N, 21·8. $C_{17}H_{17}O_8N_7$ requires C, 45·8; H, 3·9; N, 22·0%).

5-Methoxy-2-(N^3*-iso**propylguanidino**)benzoxazole* (III; R = H, R′ = OMe, R″ = Pr^i).—This was similarly prepared from 2-amino-4-methoxyphenol (0·52 g.), water (2 ml.), hydrochloric acid (0·5 ml.), and *iso*propyldicyandiamide (0·52 g.). The *hydrochloride* (0·4 g.) separated from water containing a trace of hydrochloric acid as colourless needles, m. p. 216° (Found: C, 50·9; H, 6·0; N, 19·2. $C_{12}H_{16}O_2N_4,HCl$ requires C, 50·6; H, 6·0; N, 19·6%). The *picrate* separated from aqueous ethanol in yellow needles, m. p. 204° (Found: C, 45·5; H, 3·9; N, 19·8. $C_{18}H_{19}O_9N_7$ requires C, 45·3; H, 3·9; N, 20·5%).

6-Chloro-2-(N^3*-iso**propylguanidino**)benzoxazole* (III; R = Cl, R′ = H, R″ = Pr^i).—2-Amino-5-chlorophenol (10·0 g.), *iso*propyldicyandiamide (10·6 g.), water (50 ml.), and hydrochloric acid (7·3 ml.; *d* 1·16) were refluxed (40 min.) and diluted with water (180 ml.). The precipitated oil solidified on seeding and crystallisation from water (150 ml.)–ethanol (100 ml.), with charcoal, gave the crude *benzoxazole* (2·3 g., m. p. 178—179°). It separated from aqueous ethanol in colourless prisms, m. p. 184° (Found: C, 52·3, 52·4; H, 5·1, 5·3; Cl, 14·8. $C_{11}H_{13}ON_4Cl$ requires C, 52·3; H, 5·1; Cl, 14·1%). The *picrate* separated from ethanol in yellow plates, m. p. 255° (decomp.) (Found: C, 42·2; H, 3·3; N, 20·2. $C_{17}H_{16}O_8N_7Cl$ requires C, 42·4; H, 3·3; N, 20·4%). Successive evaporation of the filtrate from this benzoxazole at room temperature gave a series of precipitates, the m. p.'s of which descended to *ca.* 140° before rising again. The last fraction (0·53 g.), m. p. 170—174°, after five crystallisations from ethanol, gave 2-amino-6-chlorobenzoxazole, m. p. 182—183°, mixed m. p. 183—184°, and mixed m. p. with the oxazole (III; R = Cl, R′ = H, R″ = Pr^i) 144—150°.

In some early experiments when the reaction mixture was refluxed for 2 hr. the dark oil which separated did not crystallise. It gave a crystalline picrate with ethanolic picric acid, and crystallisation from ethanol gave small yellow needles, m. p. and mixed m. p. 219°, of *2-amino-6-chlorobenzoxazole picrate* (Found: C, 39·7; H, 2·3; N, 16·8. $C_{13}H_8O_8N_5Cl$ requires C, 39·2; H, 2·0; N, 17·6%). This picrate was dissolved in 2-ethoxyethanol and treated with *n*-propanolic hydrogen chloride followed by dry ether. The corresponding *hydrochloride* was precipitated, and was obtained as a colourless solid, m. p. 208°, by reprecipitation from propanol by ether (Found: C, 40·7; H, 3·1; N, 12·7. $C_7H_6ON_2Cl_2$ requires C, 40·9; H, 2·9; N, 13·6%). The free *base* separated from aqueous ethanol in colourless prisms, m. p. and mixed m. p. 184° (Found: C, 49·9; H, 2·9. $C_7H_5ON_2Cl$ requires C, 49·9; H, 3·0%).

2-Amino-6-chlorobenzoxazole.—2-Amino-5-chlorophenol (1·44 g.) in ethanol (5 ml.) was added to cyanogen bromide (1·06 g.); the mixture darkened and became warm. After 2 days at room temperature warm water was added to dissolve the crystalline precipitate, followed by aqueous sodium hydroxide. *2-Amino-6-chlorobenzoxazole* (1·40 g., 83%) was precipitated and separated from aqueous ethanol in pale yellow rhombs, m. p. 184° (Found: C, 50·0; H, 3·0; N, 15·8%),

depressed to ~145° on admixture with 6-chloro-2-(N^3-*iso*propylguanidino)benzoxazole. The *picrate*, yellow needles from aqueous ethanol, had m. p. 219° (Found: C, 39·1; H, 2·1%).

m-*Chlorophenol*.—*m*-Chloroaniline (161 g.) was diazotised according to Fieser and Thompson's method [10] and the solution added dropwise to a mixture of water (520 ml.), sulphuric acid (540 ml.; *d* 1·84), and copper sulphate pentahydrate (150 g.) that was being steam-distilled. The temperature of the diazotised solution was kept below 5° until immediately before the addition. Extraction of the distillate (5—6 l.) with ether, followed by distillation, gave the phenol (70—75% yield), b. p. 210—214°, deliquescent yellow needles, m. p. 31—32°.

1 : 2-*Dichloro*-4 : 5-*dinitrobenzene*.—This was prepared according to Turner and Le Fèvre's method [16] and the crude product crystallised twice from glacial acetic acid–water (4·5 : 1 by volume). The product separated in colourless plates, m. p. 110°, and showed the following absorption maxima in the 11—13 μ region: 11·10, 11·34, 11·73, and 12·77 μ.

4 : 5-*Dichloro*-2-*nitrophenol*.—1 : 2-Dichloro-4 : 5-dinitrobenzene (1·2 g.) was refluxed with sodium hydroxide (0·4 g.) in water for 5 hr. Acidification of the deep red solution precipitated the *nitrophenol* (1·0 g.) which crystallised from aqueous ethanol as yellow prisms, m. p. 68° (Found: C, 34·9; H, 1·6; N, 6·8; Cl, 33·9. $C_6H_3O_3NCl_2$ requires C, 34·6; H, 1·4; N, 6·7; Cl, 34·0%). Its infrared absorption spectra showed maxima at 11·20, 11·41, 11·64, 11·85, and 13·17 μ. Woolley and Pringle [17] report m. p. 70—71° but give no preparative details.

2-*Amino*-4 : 5-*dichlorophenol*.—Sodium dithionite (16 g.) in water (50 ml.) was added gradually with shaking to 4 : 5-dichloro-2-nitrophenol (4·2 g.) in hot water (20 ml.) and ethanol (50 ml.). The ethanol was distilled off and, on cooling, the aminophenol (3·0 g., 84%) was precipitated. Crystallisation from water gave colourless needles, m. p. 171—172° (Found: C, 40·5; H, 3·0; N, 7·7; Cl, 39·4. Calc. for $C_6H_5ON_2Cl_2$: C, 40·4; H, 2·8; N, 7·9; Cl, 39·9%). Its infrared absorption spectra showed maxima at 11·13, 11·55, 11·64, and 12·52 μ. Woolley and Pringle [17] give m. p. 174—175° and used the less convenient reduction by tin and hydrochloric acid.

3 : 4-*Dichloronitrobenzene*.—This was prepared from *o*-dichlorobenzene [18] and had m. p. 42°. It showed infrared absorption maxima at 11·31, 12·11, 12·56, and 12·97 μ.

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[16] Turner and Le Fèvre, *J.*, 1927, 1119.
[17] Woolley and Pringle, *J. Biol. Chem.*, 1952, **194**, 729.
[18] McMaster and Magill, *J. Amer. Chem. Soc.*, 1928, **50**, 3038.