190. *Phthalocyanines. Part XII. Experiments on the Preparation of Tetrabenzporphyrins.*

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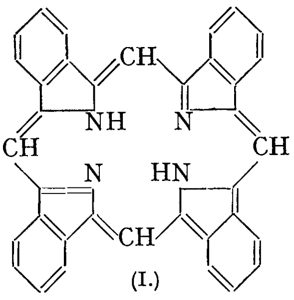
The porphyrazines of Part XI (preceding paper) bridge one gap between phthalocyanines and porphyrins. The connection between the two series would be strengthened by the isolation of tetrabenzporphin (I) in which the pyrrole rings of porphin carry benzene rings fused to the β-carbon atoms. The close resemblance which this compound bears to phthalocyanine in molecular complexity would be expected to be reflected in a similarity in general properties, although differences in absorption spectra and basicity might be anticipated. This paper describes several unsuccessful attempts at its synthesis.

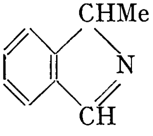
The methods elaborated by Hans Fischer for the synthesis of porphyrins all involve the use of substituted pyrroles or of dipyrrylmethenes, themselves prepared from pyrroles.

The corresponding parent ring system for the present investigation is the *iso*indole. The simple bases of this series are extremely unstable and formed with difficulty, if at all * (Gabriel and Neumann, *Ber.*, 1893, **26**, 521, 705, 952; Malan and Robinson, J., 1927, 2653; Fenton and Ingold, J., 1928, 3295).

The corresponding dihydro-compounds, although not very stable, are comparatively easily made (Gabriel and Neumann, *loc. cit.*; Scholtz and co-workers, *Ber.*, 1898, **31**, 414, etc.; von Braun and co-workers, *Ber.*, 1913, **46**, 1790; 1926, **59**, 2330) and many oxygenated derivatives such as phthalimide and phthalimidine are stable substances. A convenient starting material for the synthesis of tetrabenzporphin appeared to be available in the 1-methyl-ψ-*iso*indole (II) of Gabriel and Neumann (*loc. cit.*, p. 709). It was hoped that the methyl groups of this would supply the four linking methene groups of (I).



(I.)



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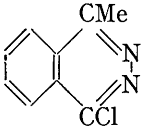
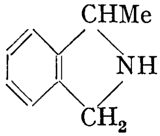


(III.)



(IV.)

A difficulty, however, arose in the preparation of the base. Gabriel and Neumann reported that 4-chloro-1-methylphthalazine (III), on reduction with zinc and hydrochloric acid,

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* In an attempt to confirm the presence of the *iso*indole ring in phthalocyanine we distilled this with zinc dust. The products were benzonitrile, phthalonitrile, and ammonia. Indications of the presence of a trace of an *iso*indole base were obtained. The experiment resembles somewhat those of Gabriel (*Ber.*, 1880, **13**, 1685) and Bamberger (*ibid.*, 1888, **21**, 1888) on the zinc dust distillation of phthalimide, which yielded a trace of an *iso*indole base, probably a dihydro-base.

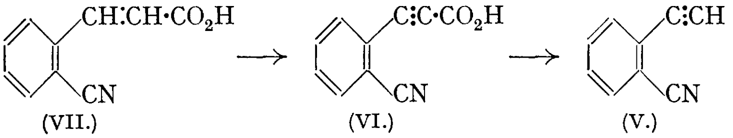
yielded 1-methyl-ψ-*iso*indole (II), whereas the use of tin and hydrochloric acid carried reduction to the dihydro-stage (IV). The parent base (II) was characterised and analysed by them as the double zinc chloride, the platinichloride, and the picrate, the dihydro-base (IV) as the hydrochloride (m. p. 170°) and nitrosoamine (m. p. 98°).

Fenton and Ingold (*loc. cit.*), who used the same preparative methods, describe the picrate of (II) as decomposing from 135° upwards, and the picrate of the dihydro-base as melting at 151°. We have carefully repeated these reductions and can find no evidence for the formation of methyl-ψ-*iso*indole. In our hands the product from the reduction of 4-chloro-1-methylphthalazine by both of Gabriel's methods was the dihydro-base (IV) and yielded the same hydrochloride (m. p. 170°), methiodide (m. p. 125°), and nitrosoamine (m. p. 100°). The picrate of the base made by reduction with zinc melted at 150°. Mixtures of the derivatives of the base made by the two methods showed no depression of melting point. Gabriel's analytical figures were obtained with derivatives containing large added groups and the effect of the two atoms of hydrogen was masked. Our analyses of the free base, made by zinc reduction, corresponded with those required for the dihydro-compound. Moreover, the base, however prepared, was extracted from a petroleum solution by aqueous sodium dihydrogen phosphate. By analogy with Willstätter's work, this would be expected of the dihydro-base, but not of methyl ψ-*iso*indole itself. It may also be pointed out that Gabriel and Neumann (*loc. cit.*, p. 526) themselves showed that the reduction of 4-chlorophthalazine with zinc and hydrochloric acid yielded dihydro*iso*indole and not ψ-*iso*indole itself. There seems no reason why the methyl group should modify the course of this reduction.

The reduction of 4-chloro-1-methylphthalazine by metal and acid therefore gives methyldihydro*iso*indole.* Similarly, Fenton and Ingold (*loc. cit.*) observed that alkaline degradation of the *p*-toluenesulphonyl derivatives of dihydro*iso*indoles yielded not the expected ψ-*iso*indoles but their dihydro-derivatives. There therefore appears to be no valid evidence for the existence of ψ-*iso*indole and its simple (unreduced) derivatives, and the abrupt contrast with pyrrole is of considerable theoretical interest (Ingold, J., **1933**, 1127).

There seemed a speculative possibility of converting 1-methyldihydro*iso*indole into a tetrabenzporphyrin by direct oxidation of the base or its salts, particularly in the presence of metals capable of yielding complex metallic compounds. The base is indeed very readily oxidised, even by atmospheric oxygen—it cannot be isolated by evaporation of its solutions in organic solvents without special precautions—but no products of the desired type could be prepared in this way. Attempts were therefore made to effect the oxidation indirectly by bromination, followed by elimination of hydrogen bromide. The only recognisable product obtained in this way was 1-*methyldihydro*iso*indole hydrobromide.*

We also examined the action of metallic reagents on o-*cyanophenylacetylene* (V), which from its structural resemblance to phthalonitrile might be expected to reproduce the exceptional reactivity of this compound. It was made by decarboxylating *o*-cyanophenylpropiolic acid (VI), itself prepared from the *dibromide* of *o*-cyanocinnamic acid (VII).



(VII.) (VI.) (V.)

Neither the cyano-acetylene (V) nor the acids of associated structure, however, reacted with metallic reagents in the desired way. The acetylene (V) also failed to condense with its own copper derivative.

Many of the attempts described above gave very intractable products. Hence it is not possible to exclude the formation of tetrabenzporphyrins with complete certainty. Nevertheless it is clear that there is no pronounced tendency for their formation from the

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* Professor C. K. Ingold, to whom these facts were communicated privately, agrees that there is now no reason to suppose that the two bases obtained in the earlier work were not the dihydro-compounds in different degrees of purity. The new facts rather strengthen than otherwise the general inferences in Fenton and Ingold's paper.

intermediates mentioned in this paper, in any way comparable with that which is shown for the preparation of phthalocyanines.

EXPERIMENTAL.

1-*Methyldihydro*iso*indole and Related Compounds.*—A solution of 30 g. of 4-chloro-1-methylphthalazine (Gabriel and Neumann, *Ber.*, 1893, **26**, 705, 952) in 200 c.c. of 20% hydrochloric acid was treated during 30 minutes with 50 g. of zinc turnings, after the addition of 5 c.c. of concentrated hydrochloric acid the mixture was kept for an hour, then made strongly alkaline with 130 g. of caustic soda in 50% solution and distilled in steam. The distillate was extracted with purified light petroleum (b. p. 40—60°), the extract dried over anhydrous potassium carbonate, and the solvent removed in an atmosphere of nitrogen. The residue was distilled under reduced pressure in a current of nitrogen. Access to the air was avoided as far as possible, nitrogen being admitted to the apparatus when the receivers were changed. A repeatable yield of 9 g. (40%) of methyldihydro*iso*indole, b. p. 94°/6 mm., 102°/15 mm., was obtained (Found : C, 80·9; H, 8·2. Calc. for $C_9H_{11}N$: C, 81·2 ; H, 8·3%. Calc. for C_9H_9N : C, 82·5; H, 6·9%). For this analysis, the freshly distilled base was transferred rapidly to a nitrogen-filled bulb. The free base and its solutions rapidly turned red when exposed to the air. If ether was used as an extracting solvent in place of petroleum and no nitrogen was used during its removal, the dark red viscous residue contained none of the base, owing to oxidation, probably through the action of peroxide in the ether.

The *hydrochloride*, m. p. 170°, was best obtained by passing dry hydrogen chloride over the ice-cold base in the absence of air, and removing the excess of base by rubbing with light petroleum (Found : Cl, 20·75. $C_9H_{11}N,HCl$ requires Cl, 20·95%). The reaction did not proceed so well in aqueous or alcoholic solution. The base readily reacted with alkyl halides either alone or in alcoholic or petroleum solution. The compounds with ethyl iodide and ethyl bromide melted respectively at 152° and 150°.

4-Chloro-1-methylphthalazine (25 g.) was heated on the steam-bath with an excess of tin and concentrated hydrochloric acid (250 c.c.) for 4 hours, and for another 4 hours after the addition of more acid (100 c.c.). The product, worked up in the manner described for the reduction with zinc, yielded 7 g. (38%) of methyldihydro*iso*indole, b. p. 108—110°/25 mm. This gave a hydrochloride, m. p. 170°, methiodide, m.p. 126°, and nitrosoamine, m. p. 100°, the m.p.'s of which were not depressed by admixture with the corresponding derivatives of the zinc reduction product.

1·5 G. of the base were completely removed from its solution in 25 c.c. of petroleum (b. p. 40—60°) by extraction with 25 c.c. of water containing 10 g. of sodium dihydrogen phosphate. The base could be recovered by making the aqueous solution alkaline and extracting it with petroleum.

Reactions with Oxidising Agents and Metals.—After methyldihydro*iso*indole had been distilled, particularly under oxidising conditions, a reddish-brown semi-solid residue remained. This yielded a purple solution in acid which deposited a precipitate on basification. After extraction with benzene and evaporation the solid yielded a reddish-brown intractable powder containing about 13% of oxygen (Found : C, 71·9 ; H, 6·6 ; N, 8·2%). A similar product was obtained by oxidation of the base in aqueous solution. Red oxidation products were also formed from the interaction of the base and cuprous chloride, and with anhydrous cupric and ferric chlorides. Zinc chloride in β-methylnaphthalene gave a purplish-blue colour at 80—120°, but no definite coloured compound could be isolated.

After a number of preliminary experiments with bromine, a crystalline product was obtained in the following way. A solution of 10·5 g. of methyldihydro*iso*indole in 52 c.c. of glacial acetic acid was treated slowly in ice with 13·5 g. of bromine dissolved in 53 c.c. of glacial acetic acid. The mixture was kept for an hour, and the solvent removed over alkali in a vacuum desiccator. The crystalline product was drained on a porous tile, and a highly brominated impurity removed by Soxhlet extraction with petroleum. This contained 50·7% of bromine, probably partly in the nucleus. The residue, which was very soluble in alcohol and water, was crystallised twice by evaporating its aqueous solution. It formed long needles, m. p. 160°, and was identified as 1-*methyldihydro*iso*indole hydrobromide* by analysis (Found : Br, 37·6. $C_9H_{11}N,HBr$ requires Br, 37·4%) and by conversion into the base (nitrosoamine, m. p. and mixed m. p. 98°).

Degradation of Phthalocyanine.—An intimate mixture of 4 g. of pure phthalocyanine and 20 g. of zinc dust was heated cautiously in a current of nitrogen. At a bath temperature of 270—350°, a red deposit formed on the cold parts of the tube. At 350—470° a small quantity of a crystalline sublimate (phthalonitrile) was formed. There was little decomposition, however, until the mixture was heated to dull redness with a free flame; ammonia, benzonitrile—identified by hydrolysis to benzoic acid—and phthalonitrile—identified by m. p., mixed m. p., and conversion into sodium phthalocyanine—were then evolved freely. The red deposit first formed probably corresponded to the formation of a trace of an *iso*indole derivative, but could not be obtained in quantity sufficient for examination.

o-*Cyanophenylacetylene* (V).—*o*-Cyanocinnamic acid (VII) was prepared by isomerisation of the sodium salt of α-nitroso-β-naphthol in boiling nitrobenzene, essentially by the method of Davies and Poole (J., 1927, 2661). It was found convenient to dry the acid first by azeotropic distillation with benzene (5 vols.) and finally over sulphuric acid in a vacuum desiccator. It formed leaflets, m. p. 255°, from alcohol (yield, 40%). Ethyl phthalate and naphthalene were far inferior as media for the isomerisation, giving yields of only about 20%. The preparation of this acid from *o*-aminocinnamic acid or its ethyl ester by the Sandmeyer reaction was much less satisfactory. The acid was left in the dark in a desiccator over an equal weight (slight excess) of bromine. After 3 days the vapour was completely absorbed and the *dibromide* was freed from adsorbed bromide in a vacuum desiccator. It was a yellow powder, m. p. 184—186° (decomp.) (Found: Br, 47·9. $C_{10}H_7O_2NBr_2$ requires Br, 48·1%).

Several methods were tried for the complete debromination of this compound, but under the optimum conditions the desired *o*-cyanophenylpropiolic acid (VI) was always contaminated with a large amount of 1-*bromo*-2-o-*cyanophenylacrylic acid*. The mixture could, however, be used for the preparation of *o*-cyanophenylacetylene. The best results were obtained as follows: 10 g. of the dibromo-acid were kept for 8 hours with 10% aqueous potassium hydroxide (2½ equivs.). The recovered acid, which contained bromide, was similarly treated for a further 24 hours, and the acid was again regenerated and finally treated with 25% caustic potash solution (2½ equivs.) for 24 hours. After regeneration and crystallisation from benzene it had m. p. 140—142° and an equivalent weight 228·2, corresponding to about 70% of the monobromo-acid. 20% Aqueous caustic soda gave a similar result, and alcoholic potash a rather worse one. Heating resulted in hydrolysis of the cyano-group. The 1-bromo-2-*o*-cyanophenylacrylic acid was isolated from the mixtures by crystallisation from water. It formed needles, m. p. 156—158° (Found: N, 5·85; equiv., 249·5. $C_{10}H_6O_2NBr$ requires N, 5·6%; equiv., 252).

The mixture of acids, containing 25—30% of *o*-cyanophenylpropiolic acid, was boiled under reflux for 24 hours with 10 vols. of water, and the product distilled in steam, the same condenser, which already contained some of the acetylene, being used. o-*Cyanophenylacetylene* separated from the distillate and more was obtained by extraction with ether. It formed white needles, m. p. 76° (Found: N, 11·0. C_9H_5N requires N, 11·0%). The yield was only 25% allowing for the impurity in the starting material, and much resin was formed. The product formed a white silver and a yellow copper derivative by the usual methods.

Attempts to prepare *o*-cyanophenylacetylene from *o*-aminophenylacetylene (v. Baeyer and Landsberg, *Ber.*, 1882, **15**, 60; v. Baeyer and Bloem, *Ber.*, 1884, **17**, 964) yielded only tarry products.

o-Cyanophenylacetylene and the mixture of *o*-cyanophenylpropiolic acid and bromocyanophenylacrylic acid yielded no sign of the formation of a stable pigment when heated under the usual conditions with the following reagents, there being only gross decomposition: metallic sodium, sodium ethoxide and amyloxide, magnesium metal and oxide, copper and both its chlorides, zinc chloride, ferric chloride.

The following related intermediates were prepared for testing for the formation of simple phthalocyanines (compare J., 1934, 1034). *o*-Cyanocinnamic acid was converted into the acid chloride in 78% yield by the action of thionyl chloride in benzene. This formed needles, m. p. 95°, from light petroleum, and with ammonia gas in benzene yielded *o*-cyanocinnamamide, m. p. 203—204° (Gabriel, *Ber.*, 1916, **49**, 1608). When this was heated under reduced pressure with an equal weight of phosphoric oxide (bath at 220°), o-*cyanocinnamonitrile* distilled, b. p. 173—174°/5 mm., m. p. 108°; yield, 55% (Found: N, 18·4. $C_{10}H_6N_2$ requires N, 18·2%). The following were made by Gabriel's methods: Phthalazone (*Ber.*, 1893, **26**, 521); phthalazine from 4-chlorophthalazine (*Ber.*, 1897, **30**, 3022) and from ωω′-bisdibromo-*o*-xylene (*Ber.*, 1893, **26**, 2210; 1895, **28**, 1830); 1-methylphthalazone (*Ber.*, 1893, **26**, 952). None of these yielded phthalocyanines on treatment with the reagents described in the preceding paragraph.

We thank Imperial Chemical Industries, Ltd. (Research Council), for a grant and for gifts of chemicals.

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[*Received, April* 15*th*, 1937.]