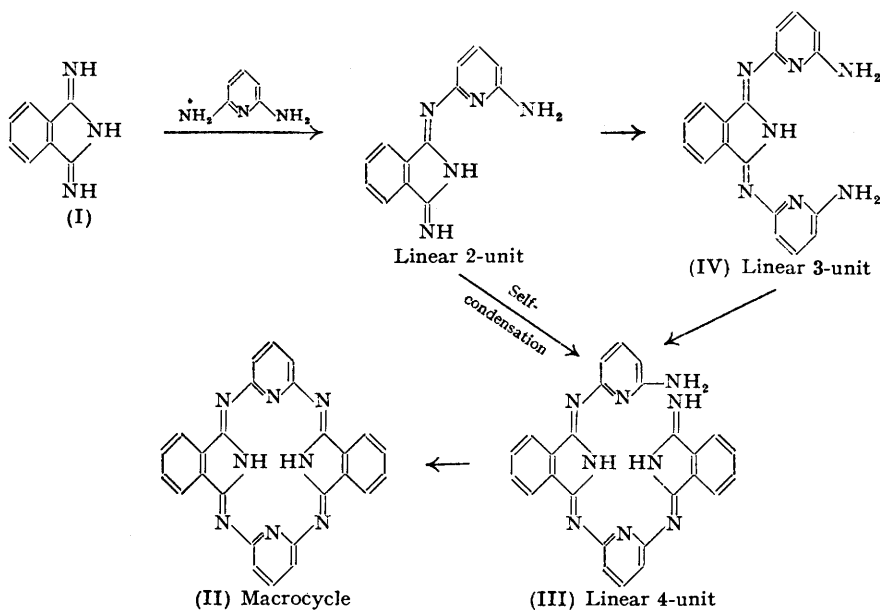


976. *Conjugated Macrocycles. Part XXIV.\* A New Type of Cross-conjugated Macrocyclic, related to the Azaporphins.*

By J. A. ELVIDGE and R. P. LINSTEAD.

1 : 3-Di-iminoisoindoline readily reacts with 2 : 6-diaminopyridine, to give a red compound,  $C_{26}H_{16}N_8$ . The structure of this has been established as (II) by analytical and synthetical evidence. It contains a cross-conjugated macrocyclic system of a novel type, related to some extent to the azaporphins. The macrocyclic compound forms metallic derivatives of high thermal stability, in which the metal occupies the centre of the ring. Light-absorption data are discussed.

THE discovery (preceding paper) that both the imino-groups of 1 : 3-di-iminoisoindoline (I) could react with primary amines opened up the prospect of constructing entirely new types of macrocycle. For example, reaction of two mols. of the di-imine with two of *m*-phenylenediamine or of an equivalent heterocyclic compound could possibly give rise by elimination of 4 mols. of ammonia to a macrocycle such as (II); and the molecular dimensions appeared not unfavourable. Such a synthesis would, of course, go through a series of steps, two possible routes being shown below (2 : 6-diaminopyridine as the *m*-diamine) :



Two difficulties which were expected were : first, that the intermediate products of the reaction might have unfavourable configurations about one or more of the C:N links



(cf. A and B). This could lead to linear polycondensation products containing more than 4 units. Secondly, the reactivity of the amino- and imino-groups would diminish as the chain grew.

\* Part XXIII, *J.*, 1952, 4846.

In fact, the formation of macrocycles by this kind of reaction proceeds remarkably easily, and we have prepared a number of compounds of the general type. The present paper describes the first substance of the class, with the structure (II), which was obtained from 2:6-diaminopyridine. When this base was heated with 1:3-di-imino*iso*indoline (I) in boiling butanol, ammonia was evolved and a sparingly soluble solid separated. No phthalocyanine was formed. Crystallisation of the product from hot nitrobenzene gave orange-red prismatic needles, m. p. 344°. The yield of pure product was about 40%; the by-products have not been examined but are probably open-chain materials of related structure. Analyses and ebullioscopic determination of its molecular weight showed the red compound to have the formula  $C_{26}H_{16}N_8$ . Although very stable to heat the compound was comparatively labile to acids, and concentrated hydrochloric acid converted it into phthalimide and 2:6-diaminopyridine in high yields and equivalent proportions.

The macrocyclic structure (II) follows unequivocally from the following facts. The formation of the red compound is represented stoichiometrically as  $2C_8H_7N_3 + 2C_5H_7N_3 = C_{26}H_{16}N_8 + 4NH_3$ , and the action of acid is the hydrolysis,  $C_{26}H_{16}N_8 + 4H_2O = 2C_8H_5O_2N + 2C_5H_7N_3$ . The hydrolysis shows that *iso*indole and pyridine rings are present in the compound, and in a 1:1 ratio, that they are linked through extra-nuclear nitrogen atoms, and that the pyridine groups are opposite [as in (II)] and not adjacent. The molecular weight shows that two of each kind of nucleus are present. The 4-unit open-chain counterpart (III) of the macrocycle could confidently be excluded from the analytical evidence (p. 5011). These results are supported by those for the metallic derivatives, described later.

The reactions and properties of the new macrocycle are particularly interesting in relation to those of phthalocyanine, and of the open-chain aza-linked materials described in the preceding paper. Of special interest was the reaction with metals.

The central ring of (II) is similar in size and environment to that in phthalocyanine or the recently discovered tetrazaporphin (Linstead and Whalley, *J.*, 1952, 4839). The pyridine nitrogen atoms can perform a similar co-ordinating function to that of the second pair of *iso*indole nitrogens in phthalocyanine and, as expected, bivalent tetraco-ordinate metals capable of exhibiting planar symmetry combine with the new macrocycle to form stable derivatives of the type  $C_{26}H_{14}N_8M$  (V). Treatment of a hot nitrobenzene solution of (II) with nickel acetate dissolved in formamide or benzyl alcohol gave in good yield a nickel derivative,  $C_{26}H_{14}N_8Ni$  (V;  $M = Ni$ ). This melted without decomposition at 386° and sublimed at 300°/10<sup>-5</sup> mm. It separated from its dark brownish-green solution in nitrobenzene as bold dark-brown needles\* with a metallic lustre. The powdered solid was dark green. When the nickel compound was boiled with concentrated hydrochloric acid, the colour was discharged, nickel ion was quantitatively liberated and the usual organic fission products could be isolated in good yield (phthalimide, 1.47 mols.; diamino-pyridine, 1.66 mols.).

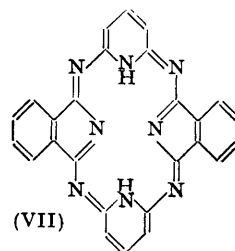
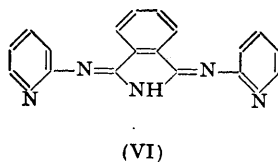
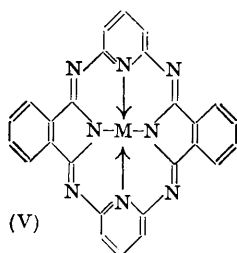
Preliminary experiments with cupric, manganous, plumbous, and mercuric acetates in place of nickel acetate showed that complex metallic compounds were formed. The copper and manganese derivatives resembled that containing nickel, but the lead and mercury compounds were orange. The lead derivative,  $C_{26}H_{14}N_8Pb$  (V;  $M = Pb$ ), separated from nitrobenzene as hair-like orange needles, melting with decomposition above 500°. Treatment of its solution in benzyl alcohol with hydrogen sulphide precipitated lead sulphide nearly quantitatively and the metal-free macrocycle (II) could be recovered from the filtrate, although not in good yield. In contrast, the nickel derivative was stable to hydrogen sulphide.

The formation of the nickel derivative is precisely what would be expected on the basis of the structure (II). In its metal complexes the macrocycle stoichiometrically resembles phthalocyanine and not the open-chain compounds such as dipyridylimino*iso*indoline

\* An X-ray examination of these crystals is being made by Dr. J. C. Speakman of the University of Glasgow, through the kindness of Professor J. Monteath Robertson, F.R.S. The substance is suitable for analysis by the heavy-atom method used for several phthalocyanines. A preliminary electron-density map fully confirms structure (V).

(VI), described in the preceding paper, which combine with only 1 equivalent of bivalent metal.

Barrett, Dent, and Linstead (*J.*, 1936, 1725) pointed out the significance of the size of the central hole in the phthalocyanine structure in relation to the metallic derivatives.



The same considerations apply to the new macrocycle. The hole is about 2.4 Å in diameter and can accommodate covalent nickel (diameter 2.1 Å) \* more readily than covalent lead (diameter 2.9 Å).\* Tetraco-ordinate lead normally displays tetrahedral symmetry, but may be planar in the new complex; possibly also electrovalent forms may make a contribution to the structure.

Two other differences have been observed between the new macrocycle and open-chain compounds such as dipyrrolyliminoisoindoline. First, it failed to react with methyl iodide, whereas the open-chain compound yields a diquaternary salt in which both pyridine nitrogen atoms are quaternised (preceding paper). Perhaps the effective difference is that the macrocyclic ring inhibits a sufficient approach of the reagent to the pyridine nitrogen atoms. Secondly, the macrocycle (II) forms a yellow monohydrate when crystallised from undried benzyl alcohol. This can be reconverted into the anhydrous orange-red form at 200° under reduced pressure. The open-chain compounds do not yield hydrates; nor do any of the metal-free azaporphins so far encountered.

The light absorption of the metal-free, lead and nickel compounds have been measured (see Table). Detailed interpretation of these values can await the accumulation of data

Compound	Solvent	$\lambda_{\max.}$ , Å	$\epsilon$	Compound	Solvent	$\lambda_{\max.}$ , Å	$\epsilon$
(II)	Morpholine †	3010	23,100	(V; M = Ni)	H·CO·NMe <sub>2</sub>	3150	27,800
		3540	20,300			3240	
(V; M = Pb)	H·CO·NMe <sub>2</sub>	2650	40,700			3640	37,800
		2790	32,300			3910	35,800
		2940	23,300			4100	31,800
		3300					
		3460					
		3650		17,500			4400

† In dimethylformamide, maxima were observed at 2800, 2900, 3240, and 3430 Å for the metal-free compound, but accurate extinction values could not be obtained owing to the very low solubility. In formic acid, maxima were observed at 3020, 3140, 3280, and 3440 Å, but the extinction coefficients fell, presumably owing to hydrolysis.

from other compounds of similar structure but two points are worth making now: (1) Formula (II) represents only one possible form of the metal-free compound; other structures such as (VII) can be written for it. In (VII) there is a large, fully conjugated ring with two imino-bridges, whereas structure (II) is only cross-conjugated. If structure (VII) made an appreciable contribution to the molecule, there would be a new chromophore and light absorption at comparatively long wave-lengths, whereas structure (II) only contains the partial chromophores present in related linear compounds, such as dipyrrolyliminoisoindoline (VI) or its diamino-derivative (IV). (2) Introduction of the metal has a marked effect both in wave-length and in intensity on the light absorption, far greater than is observed among phthalocyanines or other azaporphins (see Linstead and Whalley, *loc. cit.*; Ficken and Linstead, *J.*, 1952, 4846). A reasonable explanation seems to be that phthalocyanines are largely or completely degenerate in both the metal-free and metallic

\* These values are calculated from data given in Landolt-Börnstein (6th Edn., 1950, Vol. 1, Part 2). Pauling (*J. Amer. Chem. Soc.*, 1947, 69, 542) gives Ni 1.149 and Pb 1.538 Å, for single-bond radii in the metallic state, which are expected to be close to the values for ordinary covalent radii.

forms; hence there is little spectral change on the introduction of metal; on the other hand, the new macrocycle only functions effectively as a resonance hybrid in the form of its derivative with a metal, such as nickel, which is stable in the planar tetraco-ordinate state. In other words, in the nickel derivative a structure corresponding to (VII) plays a part; and it is this fact which brings about the change in light absorption.\* Nevertheless the hydrolysis of the nickel compound corresponds entirely to structure (V).

The main importance in the discovery of the new macrocyclic structure is that it is of a type comparatively easily prepared and capable of wide variation. Further work is in hand.

#### EXPERIMENTAL

*The Macrocycle (II).—Preparation.* 1:3-Di-iminoisoindoline (6 g.) and 2:6-diaminopyridine (4.6 g.) were heated together in boiling *n*-butanol (40 c.c.) for 8 hours, during which ammonia was evolved. The mixture was cooled, and the orange product (7.8 g.) crystallised from boiling nitrobenzene (or dry benzyl alcohol). Orange-red prismatic needles (3.5 g.), m. p. 344°, of the macrocyclic compound (II) were obtained [Found: C, 71.05; H, 3.85; N, 25.6%; *M* (ebullioscopic in nitrobenzene), 424, 453.  $C_{26}H_{16}N_8$  requires C, 70.9; H, 3.7; N, 25.4%; *M*, 440.4].

Dissolution of the red crystals in hot benzyl alcohol (undried), and cooling, afforded felted yellow needles of the *monohydrate*, m. p. 342—343° (after becoming orange-red at 150—200°) (Found: C, 68.2; H, 4.0; N, 24.1.  $C_{26}H_{16}N_8 \cdot H_2O$  requires C, 68.1; H, 4.0; N, 24.4%). When heated at 200°/10<sup>-3</sup> mm. the yellow crystals fell to a powder of the anhydrous orange-red form, m. p. unchanged (Found: N, 25.5%).

*Hydrolysis.* The macrocycle (II) (485 mg.) was stirred with warm concentrated hydrochloric acid (10 c.c.) for 10 minutes, after which the deep-red colour of the solution had faded and needle-shaped crystals began to separate. The mixture was cooled in ice and the phthalimide collected (300 mg., 1.86 mols.), m. p. and mixed m. p. 229—230°. Evaporation of the filtrate under reduced pressure yielded small needles of 2:6-diaminopyridine hydrochloride (250 mg., 1.56 mols.), characterised by conversion into (i) the base, m. p. 119—120° and mixed m. p. 120—121°, (ii) the picrate, m. p. and mixed m. p. 237—240° (decomp.), and (iii) the 3-phenylazo-derivative, m. p. 135—137° (Tschitschibabin and Seide, *J. Phys. Chem. U.S.S.R.*, 1918, 50, 522, record m. p. 137°).

*Attempted methylation.* The macrocycle (II) was recovered completely (m. p. and mixed m. p. 342—343°) after having been heated at 100° with a large excess of methyl iodide for 48 hours.

*Nickel Derivative.*—Nickel acetate (0.4 g.) in hot benzyl alcohol (20 c.c.) (or formamide) was added to a solution of the macrocycle (II) (0.6 g.) in boiling nitrobenzene (30 c.c.), and the dark brownish-green solution cooled. The *nickel* derivative (0.6 g.) crystallised from nitrobenzene as bold, dark brown needles with a metallic sheen, which crushed to a dark green powder and had m. p. 386° (Found: C, 62.9; H, 3.0; N, 22.2; Ni, 11.3.  $C_{26}H_{14}N_8Ni$  requires C, 62.8; H, 2.85; N, 22.55; Ni, 11.8%). The derivative sublimed slowly at 300°/10<sup>-5</sup> mm. It was unaffected by treatment in hot benzyl alcohol solution with hydrogen sulphide.

*Hydrolysis.* The nickel derivative (104.0 mg.) was treated with boiling 25% hydrochloric acid (6.5 c.c.) for 3 minutes and the solution then cooled in ice. Phthalimide separated (45.4 mg., 1.47 mols.), m. p. 229—230° and mixed m. p. 231—232°. The volume of the filtrate was made up to 50 c.c. with distilled water. A 20-c.c. portion was made just alkaline (litmus) with ammonia, 1% ethanolic dimethylglyoxime (5 c.c.) was added, followed by concentrated ammonia (a few drops), and the mixture warmed on the steam-bath for 20 minutes. The nickel dimethylglyoxime was collected, washed with water, and dried (24.2 mg.; *i.e.*, Ni, 11.8%, 1.00 atom). Treatment of a 10-c.c. portion of the filtrate from the phthalimide with an excess of saturated aqueous picric acid precipitated 2:6-diaminopyridine picrate (23.6 mg., 1.66 mols.), m. p. 237—240° (decomp.) alone and in admixture with authentic material.

*Lead Derivative.*—Plumbous acetate (0.6 g.) in hot benzyl alcohol (5 c.c.) was added to a solution of the macrocycle (II) (0.6 g.) in boiling nitrobenzene (25 c.c.) and the mixture cooled. The *lead* derivative (0.5 g.) crystallised from dry boiling nitrobenzene as silky, hair-like, orange needles, m. p. >500° (decomp.) (Found: C, 48.95, 48.6; H, 2.3, 2.7; N, 17.5.  $C_{26}H_{14}N_8Pb$  requires C, 48.4; H, 2.2; N, 17.3%).

\* A similar effect may account for the considerable effect of metal on the light absorption of the open-chain pyridyl compounds described in the preceding paper.

*Decomposition.* The lead derivative (149.2 mg.) was dissolved in hot benzyl alcohol (50 c.c.). Hydrogen sulphide (dried by syrupy phosphoric acid) was passed through the solution whilst it was allowed to cool. Next day, hydrogen sulphide was passed again for 30 minutes. The lead sulphide was collected, washed with benzyl alcohol and dry ether, and kept under reduced pressure (54.1 mg.) (Found: Pb, 31.4.  $C_{26}H_{14}N_8Pb$  requires Pb, 32.1%). The filtrate was evaporated under reduced pressure, and the residue kept at room temperature, whereupon it partly crystallised (79 mg.). Recrystallisation from nitrobenzene afforded in small quantity red prismatic needles of the macrocycle (II), m. p. and mixed m. p. 342—343°.

Micro-analyses were performed in the micro-analytical laboratory (Mr. F. H. Oliver) and spectrographic determinations in the spectrographic laboratory (Mrs. A. I. Boston) of this Department.

DEPARTMENT OF ORGANIC CHEMISTRY,  
IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,  
LONDON, S.W.7.

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