138. *Conjugated Macrocycles. Part XXVIII.* Adducts from Di-iminoisoindoline and Arylene-*m*-diamines, and a New Type of Cross-conjugated Macrocycle with Three-quarters of the Chromophore of Phthalocyanine.*

By J. A. Elvidge and J. H. Golden.

Yellow adducts are formed from 2 mols. of di-imino*iso*indoline (I) with 1 mol. of the diamines, *m*-phenylenediamine, 2 : 6-diaminopyridine, and 2 : 4-diaminotoluene. The first adduct (IV) in boiling butanol gives a mixture of the known benzene macrocycle (III) and a new red macrocycle (V), which has three "*iso*indole" units in the molecule. The macrocycles (III) and (V) are obtained separately by condensation of the adduct with *m*-phenylenediamine and with di-imino*iso*indoline. The other two adducts (IXa) and (IXb) respectively yield, under various conditions, only the known 2 : 6-pyridine macrocycle (XIa) and a related toluene macrocycle (XIb). However, the product (X), derived from the condensation of 2 mols. of di-imino*iso*indoline with one of diaminotoluene, condenses with di-imino-*iso*indoline to yield the homologous red macrocycle (XII).

Structures and stereochemistry are discussed and light absorptions given.

Metal-containing products from the new macrocycles (V) and (XII) are described.

Di-imino*iso*indoline (I) and *m*-phenylenediamine (II) condense together in boiling butanol, with evolution of ammonia, to give the yellow benzene macrocycle (III) in excellent yield.[1] Clark[1a] observed that when solutions of the two reactants (I) and (II) were mixed in the cold, a different product separated without the formation of ammonia. He found that heating of this in butanol gave a mixture of the benzene macrocycle (III) and a new red compound.

We have shown that the yellow intermediate is an adduct, perhaps best represented by the structure (IV). Similar adducts are formed from di-imino*iso*indoline (I) with 2 : 6-diaminopyridine and 2 : 4-diaminotoluene. The red compound we have identified as the aza-linked cross-conjugated macrocycle (V) in which there are one benzene and three "*iso*indole" corner units. This can conveniently be named the tri*iso*indole-benzene macrocycle. In extension, the homologous tri*iso*indole-toluene macrocycle † (XII) has been prepared and also the 2 : 4-toluene macrocycle † (XIb) in which there are two opposed toluene corner units and two *iso*indoline corners.

The new tri*iso*indole macrocycles (V) and (XII) are cross-conjugated and bear an interesting structural relation to the fully conjugated tribenzotetrazaporphin and phthalocyanine on the one hand and the cross-conjugated benzene macrocycle (III) on the other.

Adducts.—From a cold ethanolic solution of equimolecular quantities of di-imino*iso*indoline (I) and *m*-phenylenediamine (II) a yellow adduct separated slowly in about 25% yield by weight. Its elementary analysis fitted both of the formulæ $C_{14}H_{15}N_5$ and $C_{22}H_{22}N_8$ which correspond to 1 : 1 and 2 : 1 molecular associations of the components (I) and (II). The subsequent finding that better yields (50—60%) of the adduct were given by 2 : 1 mol. proportions of the reactants made the second formula the more likely. Determinations of molecular weight by a modified Barger method [2] failed to provide a decision.

However, good evidence for the C_{22} formula was subsequently obtained. The adduct was very labile to acids. Thus in ethanol with picric acid it yielded 1·88 mols. of insoluble di-imino*iso*indoline picrate, whilst with dilute hydrochloric acid it afforded 1·94 mols. of

* Part XXVII, *J.*, 1955, 3536.

† These trivial names are derived by extension of an earlier simple nomenclature.[1]

[1] Clark, Elvidge, and Linstead, *J.*, 1954, 2490.

[1a] Clark, unpublished work.

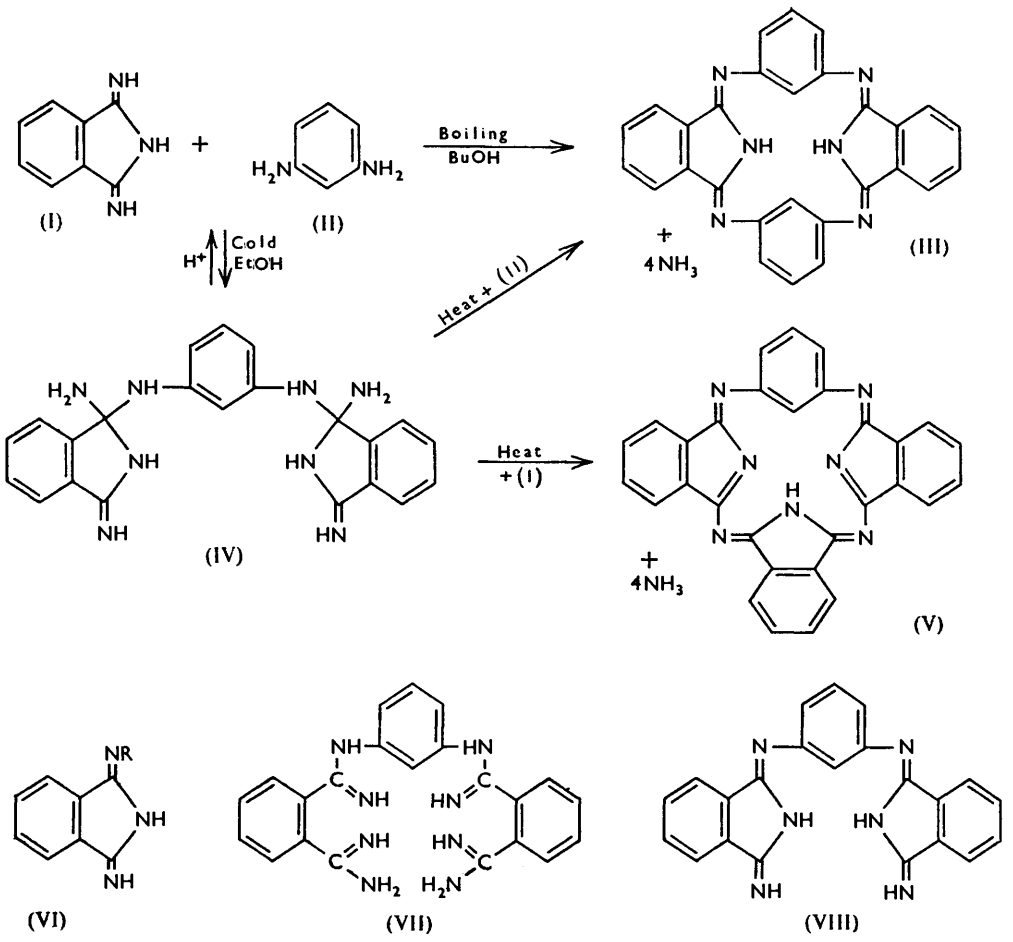
[2] Niederl, Kasanof, Kisch, and Subba Rao, *Mikrochemie*, 1949, **34**, 132.

phthalimide together with 0·91 mol. of *m*-phenylenediamine. Further, the electrometric titration characteristics of the adduct, compared with those of the separate components (I) and (II) which behave as monoacid bases, agreed with the 2 : 1 molecular association (see Table 1).

TABLE 1. *Electrometric titrations at* M/800 *in* 80% *2-methoxyethanol with* N/20-HCl *in the same solvent.*

Compound	Equivs. of acid added to reach inflexion	pK_a
(I)	1	7·47
(II)	1	4·88
Adduct from (I) and (II)	2, 3	7·40, 4·87

Moreover, di-imino*iso*indoline (I) and the *m*-diamines, 2 : 6-diaminopyridine and 2 : 4-diaminotoluene, formed similar adducts for which the elementary analyses were in unambiguous agreement with 2 : 1 molecular compositions. These were supported by mild



hydrolysis of each adduct to 2 mols. of phthalimide and 1 mol. of diamine. Additionally, the adduct from 2 : 6-diaminopyridine was split in ethanol by picric acid to give 2 mols. of the di-imine picrate.

Di-imino*iso*indoline (I) did not form adducts in the cold with other amines examined. Thus *m*-aminoacetanilide, aniline, and β-naphthylamine afforded only the known

mono-condensation products (VI; R = *m*-C_6H_4·NHAc, Ph, and 2-$C_{10}H_7$, respectively).[3,4] 2 : 7-Diaminonaphthalene with the di-imine likewise yielded a monocondensation product (VI; R = $C_{10}H_6$·NH_2), the structure of which followed from (1) its hydrolysis to 2 : 7-diaminonaphthalene and phthalimide in equivalent quantities, and (2) its self-condensation in boiling ethanol to the naphthalene macrocycle [1] (XI; R = 2 : 7-naphthylene). Inability to form adducts resulted, also, from modification of the di-imine component, and 1-imino-3-phenyliminoisoindoline (VI; R = Ph) failed to interact with *m*-phenylenediamine at room temperature.

The fine structure of the yellow adduct from di-iminoisoindoline and *m*-phenylenediamine seemed best represented as (IV). By analogy, the adducts from 2 : 6-diaminopyridine and 2 : 4-diaminotoluene are given the structures (IXa and b).

Alternatives to structure (IV) were the open-chain di-amidine tautomer (VII), and molecular complex structures, either of the naphthalene picrate or the quinhydrone type, but these were discounted. Thus the di-amidine (VII) should not be split easily to the compounds (I) and (II) by mild acid treatment. Rather would it be expected to cyclise to the imidine derivative (VIII), analogously to the ready cyclisation of succindiamidine dihydrochloride to succinimidine hydrochloride.[5] The molecular complex structures for the adducts were militated against by their ultraviolet absorptions (see Table 2), which are neither summation nor complicated spectra. The infrared absorption is of little help, structurally: Table 3 includes infrared data for the compound (VI; R = Ph) for comparison.

TABLE 2. *Ultraviolet and visible light absorptions.*

Compound	Solvent	$\lambda_{max.}$ (Å)	$E^{1\%}_{1cm.}$	ε	Compound	Solvent	$\lambda_{max.}$ (Å)	ε
(I)	MeOH	2510 } [4] 2560 }	860	12,500	(X)	MeOH	2250	68,100
							2580	28,400
		3030	318	4,600			3280 } 3400 }	9,500
(II)	,,	2420 [10]	925	10,000				
		3030	278	3,000	Toluene macrocycle (XIb)	EtOH	2260	83,900
Adduct from (I) and (II), (IV)	,,	2420	850	33,800			2470	41,000
		2920 *	212	8,400			3300	19,100
2 : 6-Diaminopyridine	,,	2470	—	7,700	Benzene macrocycle (III)	MeO·$[CH_2]_2$·OH	2280 †	77,200
		3120	—	8,200			2620	35,200
Adduct (IXa)	,,	2470	—	38,000			3340	19,200
		3040 *	—	16,000	Triisoindole macrocycles :			
(IXb)	,,	2500	—	33,400				
		3010 *	—	11,500	(V)	$CHCl_3$	2600	51,100
(VI; R = $C_{10}H_6$·NH_2)	,,	2400	—	68,400			3445	35,000
		3530	—	11,700			5070	5,300
(VIII) [6]	EtOH	2260	—	65,500	(XII)	,,	2620	49,400
		2550	—	31,300			3500	36,700
		3050	—	12,700			5420	6,100
		3460	—	9,100				

* Tailing into the visible causes the yellow colour. † Cf. ref. 1.

The chemical properties of the adducts were not inconsistent with the structures (IV), (IXa), and (IXb).

In the absence of acid, the adduct (IV) was comparatively stable, and after it had been heated in boiling ethanol for 1·5 hr., 32% was recovered. In contrast, when a 2 : 1 *mixture* of the components (I) and (II) was heated similarly, ammonia was rapidly evolved, and subsequently some benzene macrocycle (III) and the 3-unit condensation product [6] (VIII) were isolated. The adduct (IXb) from diaminotoluene was evidently less stable and more ready to eliminate the elements of ammonia than the phenylenediamine adduct (IV). An

[3] Clark, Elvidge, and Golden, *J.*, 1956, 4135.
[4] Clark, Elvidge, and Linstead, *J.*, 1953, 3593.
[5] Pinner, *Ber.*, 1883, **16**, 352; see Elvidge and Linstead, *J.*, 1954, 442.
[6] Baguley and Elvidge, following paper.

ethanol solution containing 2 mols. of di-imino*iso*indoline (I) and 1 mol. of 2 : 4-diaminotoluene deposited the yellow adduct (IXb), $C_{23}H_{24}N_8$, in only 6% yield in 2 days, but during the next week the 3-unit condensation product (X), $C_{23}H_{18}N_6$, separated in good yield. The structure of the latter was confirmed by the similarity of its light absorption to that of compound (VIII) (Table 3) and by its hydrolysis to 2 mols. of phthalimide and 1 mol. of 2 : 4-diaminotoluene.

TABLE 3. *Infrared absorptions* (*Nujol mulls*).

Compound	Principal max. (cm.$^{-1}$)	Assignment
(I)	3145, 3106	NH stretching, H-bonded . . . (i)
	1626, 1597, 1527	C:N stretching, Ph in-plane vibration, NH deformation . . . (ii)
	1304, 1256, 1213, 1170, 1152, 1131, 1060, 1009, 875, 840, 772, 705, 691	
Adduct (IV) ...	3356, 3155	NH_2, NH stretching
	1643, 1603, 1527	(ii)
	1344, 1326, 1307, 1251, 1195, 1170, 1159, 1144, 1131, 1069, 1005, 866, 840, 771, 695	
(VI; R = Ph)	3145	(i)
	1686, 1631; 1592, 1527	(ii)
	1324, 1283, 1209, 1157, 1148, 1121, 1094, 1060, 1021, 905, 830	

Macrocycles.—When the *m*-phenylenediamine adduct (IV) was heated to a higher temperature, in boiling butanol, ammonia was evolved rapidly and a dark red solid, $C_{30}H_{17}N_7$, separated in about 43% yield (by weight) : from the filtrate, the known yellow benzene macrocycle [1] (III) was isolated in comparable yield. Heating the adduct (IV) with 1 mol. of *m*-phenylenediamine (II) gave the benzene macrocycle (III) alone in 80% yield (obtained as the dihydrate), whilst heating the adduct (IV) with 1 mol. of di-imino*iso*indoline (I) produced the red compound in over 70% yield. These observations, and the elementary analysis, indicated that the red compound was the tri*iso*indole-benzene macrocycle (V) and not an open-chain compound. The cross-conjugated macrocyclic structure (V) is derived formally by the condensation $3C_8H_7N_3 + C_6H_8N_2 \longrightarrow C_{30}H_{17}N_7 + 4NH_3$, and, in agreement, hydrolysis with aqueous acid (which proceeded easily) afforded phthalimide and *m*-phenylenediamine in the molecular proportions of 3 : 1, *viz.*, $C_{30}H_{17}N_7 + 6H_2O \longrightarrow 3C_8H_5O_2N + C_6H_8N_2 + 2NH_3$ (cf. ref. 1). The molecular weight of the red compound was not obtained because of its low solubility and particularly its instability in boiling solvents. However, analogy with known cross-conjugated macrocycles [7,1] leaves little doubt that structure (V) is correct : a larger ring structure is most unlikely.

The tri*iso*indole-benzene macrocycle (V) is obtained as felted burgundy-red needles, best by rapid crystallisation from nitrobenzene. Although the macrocycle melts at 353° with decomposition, it is much less stable thermally than the symmetrical cross-conjugated macrocycles, such as (III),[1] and it decomposes more or less rapidly to tars when boiled in pyridine, morpholine, dioxan, nitrobenzene, or dimethylformamide. Unexpectedly, solutions of the macrocycle (V) in these solvents decomposed slowly even at room temperature, but in chloroform solution the macrocycle was apparently indefinitely stable. The macrocycle was also stable to acetic acid and to boiling aqueous sodium hydroxide, but it was destroyed rapidly by formic acid and by concentrated sulphuric acid.

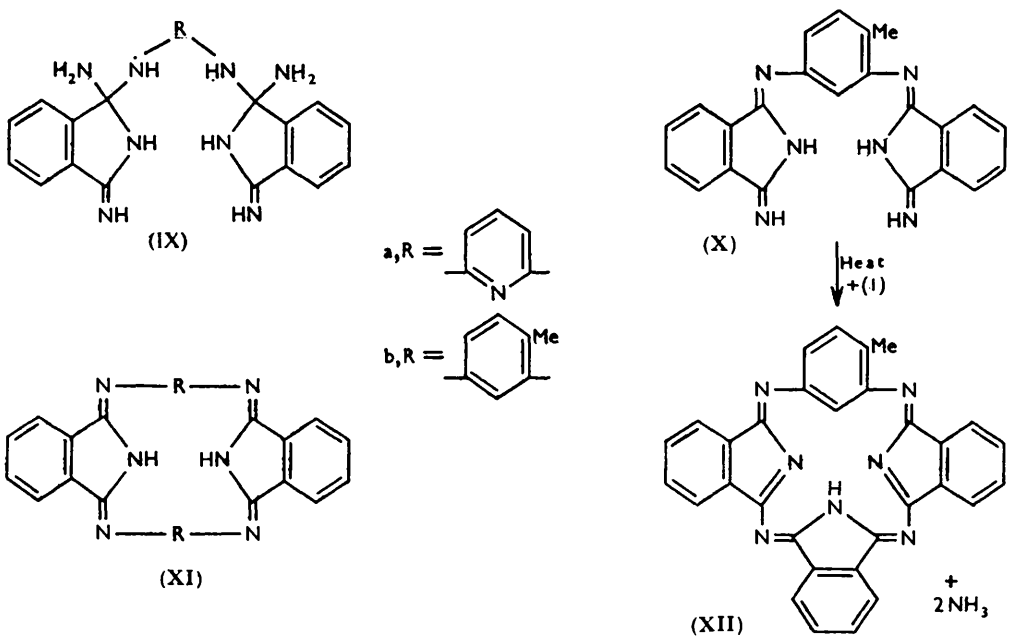
The burgundy-red colour of the new macrocycle (V) and its solutions results from a low-intensity absorption band at 5070 Å (see Table 2). This is evidently a characteristic of the aza-linked tri*iso*indole chromophore, which is in a sense three-quarters of the chromophore of phthalocyanine. However, more than a superficial comparison can hardly be made because in phthalocyanine and the related tribenzotetrazaporphin [8] this chromophore is part of a fully conjugated cyclic system.

[7] Elvidge and Linstead, *J.*, 1952, 5008.
[8] Elvidge and Linstead, *J.*, 1955, 3536.

Attempts to prepare other macrocycles of the type (V) met with only limited success. Thus, heating the 2 : 6-diaminopyridine adduct (IXa), alone or with di-imino*iso*-indoline (I), gave only the 2 : 6-pyridine macrocycle [7] (XIa). Similarly, the 2 : 4-diamino-toluene adduct (IXb) yielded only the analogous yellow macrocycle (XIb), in which opposite pairs of corner units are *iso*indoline and toluene residues. The structure of this 2 : 4-toluene macrocycle (XIb) followed from (1) its synthesis in good yield by the direct condensation of equimolecular proportions of di-imino*iso*indoline (I) and 2 : 4-diamino-toluene, (2) the elementary analysis, (3) its hydrolysis (which required moderately vigorous conditions) to phthalic acid and diaminotoluene in high yields and equivalent proportions (cf. ref. 1), and (4) the close similarity of its ultraviolet absorption to that of the benzene macrocycle (III) (see Table 2). Like the known cross-conjugated macrocycles of the type (III), the toluene macrocycle (XIb) formed solvates readily.

Thus, in contrast to the *m*-phenylenediamine adduct (IV), the adducts (IXa and b) did not react directly with di-imino*iso*indoline dissociated but very readily into their components, which then condensed together to give the most stable possible products, *viz.*, the macrocycles (XIa and b) respectively.

However, the 3-unit condensation product (X), which was formed slowly from the diaminotoluene adduct (IXb) in solution, was considerably more stable than this adduct, and in boiling butanol condensed smoothly with di-imino*iso*indoline, giving the dark red tri*iso*indole-toluene macrocycle (XII) in over 70% yield.



The macrocyclic structure (XII) for this product followed from the preparation, the elementary analysis, and the hydrolysis with aqueous hydrochloric acid to 3 mols. of phthalimide and 1 mol. of 2 : 4-diaminotoluene. This homologous macrocycle resembled the tri*iso*indole-benzene macrocycle (V) in being easily hydrolysed, in not forming solvates, and in decomposing in solvents other than chloroform. Presumably the virtually complete insolubility of the new macrocycles (V) and (XII) in boiling butanol is a protection during their preparation.

The tri*iso*indole-toluene macrocycle (XII) is a shade darker red than the lower homologue (V) as a result of a bathochromic shift of the visible absorption band to 5420 Å. This may be attributed to a hyperconjugative effect of the methyl substituent.

The stereochemistry of the two toluene macrocycles (XIb) and (XII) merits comment. If the molecules are planar, then there are two forms of the macrocycle (XIb), positionally isomeric with respect to the two methyl substituents, but only one form of the macrocycle (XII). However, an *X*-ray crystallographic study of the 2 : 6-pyridine macrocycle (XIa) has shown that its molecule is non-planar, the pyridine and *iso*indoline corner units being tilted, alternately, some 20° above and below the plane of the central hole.[9] The toluene macrocycle (XIb) would be expected to be similarly non-planar. If this is so then there are three *different* steric forms of the molecule (XIb), two of which are related as mirror images. The amorphous toluene macrocycle (XIb) may therefore be a mixture of *meso*- and racemic forms. If the tri*iso*indole-toluene macrocycle (XII) is likewise non-planar, there are two mirror-image forms, so that this macrocycle may be a racemate. The racemic forms of the macrocycles (XIb) and (XII) would be resolvable only if the mirror image forms are not readily interconvertible through a planar state.

The macrocycles and the intermediates (VI), (VIII), and (X) have potentially tautomeric molecules, and their fine structures have yet to be settled.

The formation of metallic derivatives from the tri*iso*indole macrocycles (V) and (XII) was of interest. The arrangement of nitrogen atoms about the central hole of their molecules differs from that in the porphyrins, azaporphins, and the cross-conjugated 2 : 6-pyridine macrocycle (XIa). In the new macrocycles, there is presumably only one replaceable hydrogen atom, whilst there are two tertiary nitrogens available for co-ordination with a metal atom. Nevertheless, attempts to obtain complexes from (V) incorporating the univalent metals silver and sodium were unavailing. However, highly insoluble metal-containing products were obtained by the use of cuprous cyanide and the diacetates of copper, nickel, and cobalt. Because of the insolubility and insufficient thermal stability of these products, purification by chromatography, extractive crystallisation, or sublimation was not achieved. Consequently quantitative spectroscopic data were not obtained. However, in pyridine the approximate positions of the visible absorption maxima for the cobalt derivative were obtained as 5760, $\geqslant$ 5390, 5100 Å. The elementary analyses of the products are in very rough agreement for the monometallated macrocycles, the metal content being 1—3% low. The figures for C, H, N and metal total *ca.* 100% and the C : H : N ratios approximate to the C : H : N ratio for the metal-free macrocycle. This indicates that the products are unsolvated and free from anionic residues. It appears that some metal-free macrocycle is co-precipitated with the insoluble metal complex during the preparation. This is reminiscent of the mixed-crystal formation between phthalocyanine and tribenzotetrazaporphin.[8] The precise state of combination of the bivalent metals in the complexes from the new macrocycles (V) and (XII) remains to be determined.

Experimental

Analyses were by Mr. F. H. Oliver and his staff of the Microanalytical Laboratory, and measurements of ultraviolet light absorption by Mrs. A. I. Boston and of infrared absorption by Mr. R. L. Erskine of the Spectroscopic Laboratory of this Department.

Adduct (IV) *from* m-*Phenylenediamine and Di-imino*iso*indoline.*—(a) *Preparation.* Di-imino-*iso*indoline[11] (I) (14·5 g.) was dissolved in warm ethanol (125 c.c.), and *m*-phenylenediamine (5·4 g.; freshly distilled) was added with swirling and cooling of the solution. The solution became yellow and began to deposit yellow hexagonal platelets. After 24 hr., the m-*phenylenediamine–di-*(1 : 3-*di-imino*iso*indoline*) *adduct* was collected and washed with ethanol and ether [yield 9·1 g.; m. p. 154° (decomp.)] (Found : C, 66·4; H, 6·0; N, 27·8. $C_{22}H_{22}N_8$ requires C, 66·3; H, 5·6; N, 28·1%).

(b) *Action of picric acid.* A solution of the adduct (398 mg.) in methanol (5 c.c.) was added to picric acid (458 mg.) in ethanol (10 c.c.) at 40°, whereupon a dense yellow precipitate was formed. After the mixture had been cooled in ice for 10 min., the picrate was collected, washed thoroughly

[9] Speakman, *Acta Cryst.*, 1953, **6**, 784.
[10] Grammaticakis, *Bull. Soc. chim.*, 1951, 534.
[11] Elvidge and Linstead, *J.*, 1952, 5000.

with ethanol, and dried [yield, 703 mg., 1·88 mols.; m. p. 295° (decomp.) undepressed by the picrate of di-imino*iso*indoline]. *Di-imino*iso*indoline picrate*, prepared in ethanol in 94% yield, was precipitated as yellow needles, m. p. 299° (decomp.) unchanged by crystallisation from a large volume of ethanol (Found : N, 22·8. $C_{14}H_{10}O_7N_6$ requires N, 22·5%).

(c) *Hydrolysis.* The adduct (704 mg.) was dusted into boiling 2N-hydrochloric acid (12 c.c.). The solid became red and then dissolved to a colourless solution, cooling of which to 0° afforded needles of phthalimide (507 mg., 1·94 mols.), m. p. amd mixed m. p. 233°. The filtrate was treated with an excess of aqueous sodium hydroxide, and extracted with ether for 6 hr. On evaporation of the dried (Na_2SO_4) extract, *m*-phenylenediamine (174 mg., 0·91 mol.) was obtained, identified as the picrate, m. p. and mixed m. p. 183° (conversion yield, 67%).

Adduct (IXa) *from* 2 : 6-*Diaminopyridine.*—(a) *Preparation.* A solution of di-imino*iso*indoline (I) (2·9 g.) in hot ethanol (30 c.c.) was filtered into ethanolic 2 : 6-diaminopyridine (1·09 g. in 5 c.c.). After 24 hr. at 0°, the 2 : 6-*diaminopyridine–di-*(1 : 3-*di-imino*iso*indoline*) *adduct* had separated as yellow prisms (1·1 g.), m. p. 160—161° (decomp.) (Found : C, 63·1; H, 5·4; N, 31·6. $C_{21}H_{21}N_9$ requires C, 63·1; H, 5·3; N, 31·6%).

(b) *Action of picric acid.* Addition of picric acid (500 mg.) in ethanol (25 c.c.) to a solution of the adduct (100 mg.) in ethanol (40 c.c.) precipitated di-imino*iso*indoline picrate (138 mg., 1·47 mols.), m. p. and mixed m. p. 300° (decomp.).

(c) *Hydrolysis.* The adduct (223 mg.) was warmed with 2N-hydrochloric acid (3 c.c.) for 2 min. and the resulting colourless solution cooled in ice. Needles of phthalimide separated (157 mg., 1·92 mols.), having m. p. and mixed m. p. 235°. The filtrate was made alkaline with sodium hydroxide and extracted with ether for 24 hr. Evaporation of the extract afforded 2 : 6-diaminopyridine (50·5 mg., 0·83 mol.), m. p. and mixed m. p. 118°.

Reaction of 2 : 4-*Diaminotoluene with Di-imino*iso*indoline : Adduct and Condensation Product.*—A solution of the di-imine (5·8 g.) in ethanol (45 c.c.) was mixed with the diamine (2·44 g.) in ethanol (15 c.c.). During 2 days, small yellow prisms of the 2 : 4-*diaminotoluene–di-*(1 : 3-*di-imino*iso*indoline*) *adduct* (IXb) separated (0·47 g.); they had m. p. 146—147° (decomp.) after being washed with ethanol and ether (Found : C, 66·9; H, 6·0; N, 27·0. $C_{23}H_{24}N_8$ requires C, 67·0; H, 5·9; N, 27·2%). During the next 7 days, the filtrate deposited yellow prisms of 2 : 4-*di-*(1-*imino*-3-iso*indolinylideneamino*)*toluene* (X) (4 g.), m. p. 255° (decomp.) raised to 259° (decomp.) by extractive crystallisation from benzene (Found : C, 72·6; H, 5·0; N, 22·3. $C_{23}H_{18}N_6$ requires C, 73·0; H, 4·8; N, 22·2%).

Hydrolysis of the Diaminotoluene Adduct.—Warming of the adduct (IXb) (83 mg.) with 2N-hydrochloric acid (1 c.c.) for 2 min. gave a colourless solution which soon deposited needle-shaped crystals. Filtration of the mixture, after it had been kept at 0° overnight, afforded phthalimide (48·5 mg., 1·64 mols.), m. p. and mixed m. p. 235°. The filtrate was made alkaline with aqueous sodium hydroxide and extracted with ether for 48 hr. Evaporation of the extract gave 2 : 4-diaminotoluene (17·2 mg., 0·70 mol.), m. p. and mixed m. p. 96°.

Hydrolysis of the Condensation Product (X).—During 5 min., the compound (245 mg.) reacted with hot 2N-hydrochloric acid (3 c.c.) to give a colourless solution. When cooled to 0°, this deposited phthalimide (179 mg., 1·88 mols.), m. p. and mixed m. p. 233°. From the filtrate, by addition of aqueous sodium hydroxide and extraction with ether for 24 hr., 2 : 4-diaminotoluene (75 mg., 0·95 mol.) was isolated, having m. p. 97° and mixed m. p. 99°

*Reactions of Other Amines with Di-imino*iso*indoline in the Cold.*—(a) *With* m-*aminoacetanilide.* Di-imino*iso*indoline (1 g.) and *m*-aminoacetanilide [12] (1 g.) were dissolved together in ethanol (20 c.c.). During 3 days ammonia was formed and pale-yellow needles separated. The product (0·96 g.) had m. p. 240—241° (decomp.), unchanged by crystallisation from ethanol and undepressed by 3-*m*-acetamidophenylimino-1-imino*iso*indoline [3] (VI; R = *m*-C_6H_4·NHAc), m. p. 240—241° (decomp.).

(b) *With aniline.* Aniline (0·64 g.) was added to a cold solution of di-imino*iso*indoline (1 g.) in a minimum of ethanol. After 20 hr., the deep-yellow solution (odour of ammonia) was concentrated under reduced pressure. The crystalline precipitate (0·53 g.) had m. p. 202° (decomp.) undepressed by 1-imino-3-phenyliminoisoindoline [4] (VI; R = Ph), m. p. 203° (decomp.).

(c) *With* β-*naphthylamine.* Solutions of β-naphthylamine (3 g.) and di-imino*iso*indoline (3 g.) in ethanol (15, 45 c.c. respectively) were mixed and kept at 0° for 2 days. β-Naphthylamine (0·25 g.) separated and the filtrate was concentrated under reduced pressure to 20 c.c.

[12] Jacobs and Heidelberger, *J. Amer. Chem. Soc.*, 1917, **39**, 1447.

and cooled in ice. Yellow 1-imino-3-2′-naphthyliminoisoindoline (VI; R = 2-$C_{10}H_7$) separated (1·8 g.), having m. p. and mixed m. p. 203° (decomp.).[4]

(d) *With* 2 : 7-*diaminonaphthalene.* The diaminonaphthalene (3·16 g.) was dissolved in a warm solution of di-iminoisoindoline (5·8 g.) in ethanol (55 c.c.). Overnight, diaminonaphthalene (0·85 g.) crystallised, but from the yellow filtrate, during a further 2 days, 3-(7-*amino*-2-*naphthylimino*)-1-*imino*isoindoline (VI; R = $C_{10}H_6$·NH_2) separated as yellow needles (0·36 g.), m. p. 225—226° (decomp.), which contained some ethanol of crystallisation (Found: C, 74·5, 74·7; H, 5·4, 5·2; N, 18·9. $C_{18}H_{14}N_4$,$\frac{1}{4}C_2H_5$·OH requires C, 74·6; H, 5·3; N, 18·8%).

Hydrolysis of the preceding compound (225 mg.) with boiling 2N-hydrochloric acid (4 c.c.) for 2—3 minutes, and cooling of the solution in ice, afforded phthalimide (115 mg., 0·99 mol.), m. p. and mixed m. p. 234°. The filtrate was made alkaline with sodium hydroxide whereupon 2 : 7-diaminonaphthalene crystallised and this was collected and washed with water; yield 95 mg. (0·77 mol.); m. p. and mixed m. p. 164°.

The 3-(7-amino-2-naphthylimino)-1-iminoisoindoline (470 mg.) was boiled in ethanol (25 c.c.) for 24 hr., during which ammonia was evolved and a yellow solid separated. Next day, the latter was washed with boiling ethanol and with ether, and was dried, to yield the naphthalene macrocycle (XI; R = 2 : 7-$C_{10}H_6$) (230 mg., 52%), m. p. and mixed m. p. *ca.* 500° (decomp.).[1]

Attempt to Form an Adduct from 1-*Imino*-3-*phenyliminoisoindoline* (VI; R = Ph).—*m*-Phenylenediamine (1·1 g.) was dissolved in a solution of the imidine derivative [4] (4·4 g.) in ethanol (100 c.c.). After being kept at 0° overnight, 1-imino-3-phenyliminoisoindoline (2·1 g.), m. p. 210° (decomp.), was recovered. Concentration of the filtrate and cooling afforded a second, less pure, crop of the monophenyl-imidine.

Effect of Gentle Heat on the m-*Phenylenediamine Adduct* (IV).—The adduct (500 mg.) was boiled in dry ethanol (50 c.c.) for 1·5 hr., during which ammonia was slowly evolved. The yellow solution was then concentrated under reduced pressure to 5 c.c. and cooled at 0° for 3 days. Slightly impure adduct separated (158 mg., 32%), having m. p. 135° (decomp.) and mixed m. p. 145° (decomp.).

Effect of Heat on a 2 : 1 *Mixture of Di-iminoisoindoline and* m-*Phenylenediamine.*—A mixture of di-iminoisoindoline (5·6 g.) and *m*-phenylenediamine (2·1 g., 0·5 mol.) was added to boiling ethanol (700 c.c.). Ammonia was evolved rapidly. After 2 hr., the yellow solution was concentrated under reduced pressure to a small bulk and then kept at 0°, after which a yellow crystalline solid separated [6·2 g.; m. p. 275° (decomp.) with darkening from 210°]. Several crystallisations of a portion from ethanol afforded the benzene macrocycle (III), as small yellow needles, m. p. 375° and mixed m. p. 378—380°.[1]

A second portion of the product was chromatographed in ethanol on alumina (Spence, type H), and the later eluates were collected and evaporated. From dimethylformamide–benzene, 1 : 3-di-(1-imino-3-*iso*indolinylideneamino)benzene (VIII) crystallised as golden yellow prisms, m. p. and mixed m. p. 265—270° (decomp)[6] (depending on the rate of heating) [Found: N (on air-dried material) 20·0, (on material dried at 130°/10^{-4} mm.) 22·85. Calc. for $C_{22}H_{16}N_6$,$3H_2O$; N, 20·1. Calc. for $C_{22}H_{16}N_6$: N, 23·1%].

Conversion of the m-*Phenylenediamine Adduct* (IV) *into Macrocycles.*—(*a*) The adduct (IV) (2 g.) was boiled in butanol (40 c.c.) for 24 hr. Ammonia was evolved rapidly at first, and a red solid separated [0·87 g.; m. p. 348° (decomp.)]. Several rapid recrystallisations from nitrobenzene afforded the *tri*isoindole-*benzene macrocycle* (V) as felted burgundy-red needles, m. p. 353° (decomp.) (Found: C, 76·0; H, 3·7; N, 20·6. $C_{30}H_{17}N_7$ requires C, 75·8; H, 3·6; N, 20·6%). The yellow filtrate, on cooling, slowly deposited a yellow solid (0·6 g.), m. p. 348°. Recrystallisation from ethanol gave yellow needles of the *benzene macrocycle* (III) *dihydrate*, m. p. 365° (Found: C, 70·8; H, 5·0; N, 17·3. $C_{28}H_{18}N_6$,$2H_2O$ requires C, 70·8; H, 4·7; N, 17·7%), which on sublimation at 300°/20 mm. afforded the benzene macrocycle (III), m. p. and mixed m. p. 380° [1] (Found: N, 19·4. Calc. for $C_{28}H_{18}N_6$; N, 19·2%).

(*b*) The adduct (IV) (1 g.) and *m*-phenylenediamine (0·25 g., 1 mol.) were boiled together in butanol (25 c.c.) for 20 hr. The solution remained yellow and no solid was deposited. Ether (25 c.c.) was added and the solution kept at 0° overnight. Fine yellow needles separated (0·88 g., 80%), identified as benzene macrocycle (III) by mixed m. p.

(*c*) The adduct (IV) (3 g.), di-iminoisoindoline (1·1 g., 1 mol.) and butanol (50 c.c.) were boiled together for 20 hr. Filtration of the hot solution gave the red triisoindole-benzene

macrocycle (V) which was washed with ethanol and then dried [yield, 2·65 g., 74%; m. p. 348° (decomp.)]. The reaction liquors were concentrated under reduced pressure to 10 c.c., diluted with ether (80 c.c.), and then kept overnight at 0°. Recrystallisation of the yellow precipitate from ethanol afforded yellow needles (0·36 g.) of the benzene macrocycle (III), identified by mixed m. p.

Hydrolysis of the Macrocycle (V).—The macrocycle (392 mg.) was boiled with 2N-hydrochloric acid (10 c.c.) for 5 min. and the mixture then kept at 0° overnight. Filtration yielded phthalimide (354 mg., 2·91 mol.), m. p. and mixed m. p. 233°. By addition of an excess of aqueous sodium hydroxide to the filtrate and extraction with ether for 9 hr., *m*-phenylenediamine (75 mg., 0·84 mol.) was isolated, and was then characterised as the picrate, m. p. and mixed m. p. 182°.

Conversion of the 2 : 6-*Diaminopyridine Adduct* (IX*a*) *into the Macrocycle* (XIa).—(*a*) The adduct (IXa) (1 g.) was boiled in butanol (8 c.c.) for 20 hr., during which ammonia was evolved. Cooling afforded the yellow hydrate of the 2 : 6-pyridine macrocycle (XI*a*) (0·44 g.), which was dried to the orange unsolvated form,[7] m. p. and mixed m. p. 345°.

(*b*) The adduct (IXa) (1·11 g.), di-imino*iso*indoline (0·41 g., 1 mol.), and butanol (10 c.c.) were boiled together for 20 hr. Ammonia was evolved rapidly at first and a yellow solid separated (93 mg.). The latter was dried to give the orange 2 : 6-pyridine macrocycle (XI*a*), m. p. and mixed m. p. 346°.

2 : 4-*Toluene Macrocycle* (XIb).—(a) *From the adduct* (IXb). This adduct (206 mg.) and di-imino*iso*indoline (73 mg.) were boiled together in butanol (3 c.c.) for 24 hr. Unidentified red solid (9·4 mg.) was removed and the yellow filtrate treated with ether (25 c.c.). The precipitated yellow solid (81 mg.) had m. p. 180° (decomp.), raised on recrystallisation from benzene to 318° (decomp.) undepressed by a specimen of the toluene macrocycle described next.

(b) *Conventional preparation* (cf. ref. 1). Di-imino*iso*indoline (2·9 g.), 2 : 4-diaminotoluene (2·44 g.), and butanol (50 c.c.) were heated together under reflux for 24 hr., during which ammonia was evolved. Concentration of the yellow solution to 10 c.c. and addition of ether (50 c.c.) caused precipitation of a yellow solid (2·31 g.), m. p. 210° (decomp.). Two extractive crystallisations from benzene gave the *hydrated* 2 : 4-*toluene macrocycle* (XIb) as an amorphous yellow powder (0·7 g.), m. p. 330° (decomp.) unchanged on further crystallisation from benzene (Found: C, 74·0; H, 5·2; N, 17·25. $C_{30}H_{22}N_6,H_2O$ requires C, 74·4; H, 5·0; N, 17·4%); it was partially dehydrated at 100° (Found: C, 76·1; H, 5·0; N, 17·8. $C_{30}H_{22}N_6,\frac{1}{2}H_2O$ requires C, 75·8; H, 4·8; N, 17·7%) and completely desolvated at 150°/10^{-6} mm. in 16 hr. (Found: C, 77·5; H, 4·9; N, 17·8. $C_{30}H_{22}N_6$ requires C, 77·2; H, 4·8; N, 18·0%).

(c) *Hydrolysis*. The macrocycle (XIb) (152 mg.) was heated for 2 hr. under reflux with 1 : 1 concentrated hydrochloric acid–acetic acid (5 c.c.). The clear solution was concentrated to 1 c.c. and cooled in ice. Phthalic acid separated (103 mg., 1·91 mols.), m. p. and mixed m. p. (sealed tube) 197°. An excess of aqueous sodium hydroxide was added to the filtrate, which was then extracted with ether for 48 hr. to afford 2 : 4-diaminotoluene (73 mg., 1·82 mols.), m. p. 97° and mixed m. p. 99°.

*Tri*iso*indole-toluene Macrocycle* (XII).—(a) *Preparation*. 2 : 4-Di-(1-imino-3-*iso*indolinylideneamino)toluene (X) (824 mg.) and di-imino*iso*indoline (290 mg.) were boiled together in butanol (10 c.c.). Ammonia was evolved, rapidly at first, and a red precipitate was formed. After 20 hr., the solid was collected and washed thoroughly with ethanol [yield, 700 mg., 72%; m. p. 285° (decomp.)]. Several rapid recrystallisations from nitrobenzene yielded the *tri*iso*indole-toluene macrocycle* as a dark red powder, m. p. 285° (decomp.) (Found: C, 75·8; H, 4·2; N, 19·8. $C_{31}H_{19}N_7$ requires C, 76·1; H, 3·9; N, 20·0%). No other solid product was isolated from the reaction liquors.

(b) *Hydrolysis*. The macrocycle (XII) (223 mg.) was added during 10 min. to hot 2N-hydrochloric acid (4 c.c.). On being kept cold, overnight, the colourless solution deposited phthalimide (195 mg., 2·9 mols.), m. p. and mixed m. p. 235°. The filtrate was made alkaline with sodium hydroxide solution and extracted with ether for 48 hr. Evaporation of the extract gave 2 : 4-diaminotoluene (55 mg., 0·98 mol.), m. p. 97° and mixed m. p. 99°.

Formation of Metal Derivatives.—(i) When a solution of cuprous cyanide (0·5 g.) in boiling pyridine (50 c.c.) was filtered into a boiling solution of the tri*iso*indole-benzene macrocycle (V) (0·5 g.) in pyridine (50 c.c.), dark brown needle-shaped crystals were precipitated. After the mixture had been boiled for 30 min., the insoluble, infusible, copper derivative (370 mg.) was

collected, extracted with boiling pyridine (2 × 50 c.c.), washed with ether (80 c.c.) and dried at 200°/10^{-6} mm. (Found : C, 67·4; H, 3·2; N, 18·8; Cu, 10·2. Calc. for $C_{30}H_{16}N_7Cu$: C, 67·0; H, 3·0; N, 18·2; Cu, 11·8%). (ii) Similarly, cupric acetate afforded dark brown needles of a copper derivative (Found : C, 68·7; H, 3·2; N, 18·7; Cu, 9·2%) which was unchanged by being dried at 200°/10^{-6} mm. for 12 hr. (Found : C, 68·8; H, 3·3; N, 19·2; Cu, 9·2%).

(iii) Similarly, with nickel acetate, dark brown needles of an insoluble nickel derivative were obtained (Found : C, 69·5; H, 3·3; N, 19·1; Ni, 10·5. Calc. for $C_{30}H_{16}N_7Ni$: C, 67·6; H, 3·0; N, 18·4; Ni, 11·0%).

(iv) A solution of anhydrous cobalt acetate (0·8 g.) in dry methanol (50 c.c.) was filtered into a boiling solution of the tri*iso*indole-benzene macrocycle (V) (0·8 g.) in dry benzyl alcohol. The dark purple mixture was cooled and filtered, and the solid was washed with benzyl alcohol and digested with methanol. The cobalt derivative (210 mg.) was thus obtained as fine black needles, soluble in pyridine and quinoline, but not in other solvents (Found : C, 68·2; H, 3·2; N, 18·8; Co, 8·2. Calc. for $C_{30}H_{16}N_7Co$: C, 67·5; H, 3·0; N, 18·4; Co, 11·05%).

(v) Cupric acetate (0·5 g.) in boiling pyridine (100 c.c.) was filtered into a freshly boiling solution of the tri*iso*indole-toluene macrocycle (XII) (0·5 g.) in pyridine (350 c.c.). Within 2 min., the precipitate was collected and washed with boiling pyridine (100 c.c.) and then ether (200 c.c.). The copper derivative (354 mg.) formed dark brown needles with a blue reflex (Found : C, 68·5; H, 3·4; N, 18·2; Cu, 9·8. Calc. for $C_{31}H_{18}N_7Cu$: C, 67·4; H, 3·3; N, 17·8; Cu, 11·5%).

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