Conjugated Macrocycles. Part XXV. Cross-conjugated Macrocycles with Inner Great Rings of 16, 20, and 24 Atoms.*

By P. F. Clark, J. A. Elvidge, and R. P. Linstead.

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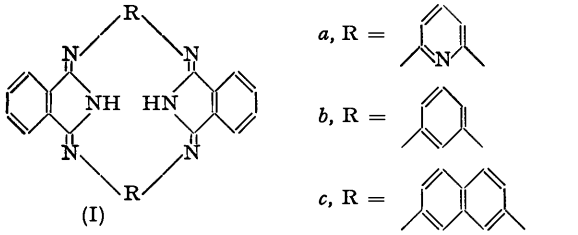
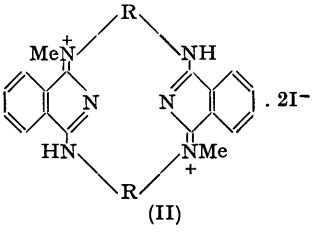
The formation of cross-conjugated macrocycles by the condensation of 1 : 3-di-imino*iso*indoline with appropriate diamines has been further studied. Thus from *m*-phenylenediamine, 2 : 7-diaminonaphthalene, and 2 : 8-diaminoacridine, the macrocycles (I*b*, *c*, and *d*) were obtained, which have 16-, 20-, and 24-membered inner great rings. With 3 : 5-diaminopyridine the reaction yields the macrocycle (I*e*). This is a positional isomer of the macrocycle (I*a*), previously prepared from 2 : 6-diaminopyridine. Unlike (I*a*), and in keeping with their structure, the new macrocycles do not co-ordinate metals centrally, though (I*e*) forms amorphous insoluble compounds with copper and zinc acetates. These may have macromolecular extended-lattice structures.

The new macrocycles have been hydrolysed quantitatively, and their light absorptions determined. The formation of compounds with mineral acids, acetic acid, and methyl iodide has been examined. The structures of the macrocycles and their salts are discussed and compared with those of related linear compounds.

A previous paper (Elvidge and Linstead, *J.*, 1952, 5008) described the formation of a novel type of cross-conjugated macrocycle (I*a*) by the condensation of 1 : 3-di-imino*iso*indoline (IV; R′ = R″ = H) with 2 : 6-diaminopyridine. As mentioned there and elsewhere (Linstead, *J.*, 1953, 2873), the reaction was a ready one and capable of extension.



(I)



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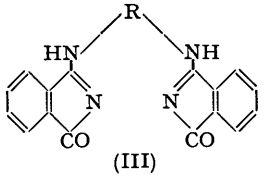

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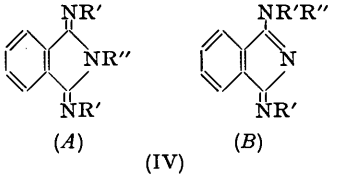


(*A*) (*B*)

(IV)

We now describe the further macrocycles (I*b*, *c*, *d*, and *e*), which we have obtained by condensing the di-imine in boiling butanol with the diamines, *m*-phenylenediamine, 2 : 7-diaminonaphthalene, 2 : 8-diaminoacridine, and 3 : 5-diaminopyridine. The yields and some characteristics of the macrocycles are given in Table 1. It is noteworthy that the naphthalene macrocycle † (I*c*), which has an inner cross-conjugated great ring of 20 atoms, is no less easily prepared than the benzene macrocycle (I*b*) and the two isomeric pyridine macrocycles (I*a*) and (I*e*), which all have 16 atoms in their inner great ring.

The related linear 3-unit compounds (III*a*—*e*) and (IV; R′ = 2-pyridyl, Ph, 2-naphthyl, and 3-pyridyl, R″ = H) have already been described (Elvidge and Linstead, *J.*, 1952, 5000; Clark, Elvidge, and Linstead, *J.*, 1953, 3593).

* Part XXIV, *J.*, 1952, 5008.

† This type of nomenclature is used in the absence of generally agreed systematic names.

The gross structure of the 2 : 6-pyridine macrocycle (I*a*) followed from its preparation, hydrolysis, and molecular formula (see *J.*, 1952, 5008). Dr. J. C. Speakman of Glasgow University examined crystals of the derived nickel complex by the *X*-ray method and obtained an electron-density projection which gave detailed confirmation of the macrocyclic structure (*Acta Cryst.*, 1953, **6**, 784; Linstead, *loc. cit.*). Interesting features of the nickel compound are (*a*) the non-coplanarity of the pyridine and *iso*indole rings with the inner great ring of the molecule, and (*b*) the bond lengths, which indicate a predominating contribution from a fully conjugated canonical form as was suggested (*J.*, 1952, 5008) on light-absorption evidence.

The new compounds now reported are given macrocyclic structures (I) by analogy with the 2 : 6-pyridine compound (I*a*). They are prepared similarly, the elementary analyses show the absence of end groups (amino or imino) which would necessarily be present in linear condensation products, and they are hydrolysed to the original diamine and phthalic acid in good yields and equivalent proportions (Table 1), which shows that equal numbers of the two units are combined alternately [as in (I)]. Determination of the molecular weights of the benzene and naphthalene macrocycles by the ebullioscopic method gave values in agreement with the 4-unit structures (I*b* and *c*). The evidence for these structures is, therefore, complete.

TABLE 1.

Macrocycle	Method of purification	Yield (%)	Form and m. p.	Mol. formula (Found)
(I*b*)	Sublimation at 340°/15 mm.	70	Long yellow needles, 380°	$C_{28}H_{18}N_6$
(I*c*)	Sublimation at 400—450°/15 mm.	70	Fine yellow needles, *ca.* 500° (decomp.)	$C_{36}H_{22}N_6$
(I*d*)	Extractive crystn. from pyridine	18	Deep yellow rods, bronze lustre, decomp. >400°	$(C_{21}H_{12}N_4)_x$ *
(I*e*)	Crystn. from hot nitrobenzene	46	Minute yellow needles, 436° (decomp.)	$(C_{13}H_8N_4)_x$ *
(I*a*) †	,, ,,	40	Orange-red laths, 344°	$C_{26}H_{16}N_8$

	Hydrolysis ‡		
Macrocycle	Necessary conditions	P	D
(I*b*)	1 : 1 conc. HCl–AcOH, 150°/7 hr.	1·90	1·79
(I*c*)	1 : 1 conc. HCl–AcOH, 180°/15 hr.	1·68	1·84
(I*d*)	Boiling conc. HCl	1·63	1·93
(I*e*)	Boiling 2N-HCl	1·78	1·64
(I*a*) †	Warm conc. HCl, 10 min.	Phthalimide, 1·86	1·56

* x undetermined, but presumably = 2, for steric reasons, and by analogy.
† Data from *J.*, 1952, 5008.
‡ P = yield of phthalic acid in mols.; D = yield of diamine (picrate) in mols.

Attempts similarly to determine the molecular weights of the acridine and 3 : 5-pyridine compounds failed, unfortunately, because of the very low general solubilities of these compounds. Comparison of the physical and chemical properties of these two compounds with those of the other products (I*a*, *b*, and *c*) leaves little doubt, however, that they have the analogous 4-unit macrocyclic structures (I*d* and *e*).

The new macrocycles are very stable thermally, particularly the benzene and the naphthalene compounds, (I*b* and *c*). These two are also resistant to hydrolysis by boiling concentrated hydrochloric acid. The acridine and the 3 : 5-pyridine macrocycle are more easily hydrolysed, but not so readily as the 2 : 6-pyridine macrocycle (I*a*). From that compound phthalimide was consequently obtained in good yield (*J.*, 1952, 5008), and not phthalic acid as in the present cases (Table 1). Qualitatively similar differences in the ease of hydrolysis were shown by the related linear 3-unit derivatives (IV; R′ = 2-pyridyl, Ph, and 2-naphthyl, R″ = H) (*J.*, 1953, 3593).

The macrocycles gave coloured solutions in cold concentrated sulphuric acid. As indicated in Table 2, addition of ice to the solutions produced in most cases coloured precipitates, presumably of the sulphates, from which the macrocycles were regenerated by alkali. The 2 : 6-pyridine macrocycle, however, was soluble in the diluted acid and

was hydrolysed to phthalimide in about 15 min. The 3 : 5-pyridine macrocycle was hydrolysed about half as rapidly.

Easier to prepare for analytical examination were the hydrochlorides. Under anhydrous conditions, the benzene and the naphthalene macrocycle (I*b* and *c*) formed orange-red and scarlet dihydrochlorides. Presumably, the basic centres are the two phthalic imidine residues in the molecules of these compounds. The 3 : 5-pyridine macrocycle (I*e*) formed a salmon-pink dihydrochloride when treated with dilute hydrochloric acid. This is presumably a dipyridinium dichloride. Difficulty was experienced in preparing a stoicheiometric salt from the highly insoluble acridine macrocycle (I*d*), and dark red products containing between 1 and 3 mols. of hydrogen chloride were obtained. All the hydrochlorides were very stable thermally.

TABLE 2.

Macrocycle	Colour of solution in conc. H_2SO_4	Effect of adding ice (and alkali)
(I*b*)	Yellow	Orange ppt. $\xrightarrow{\text{alkali}}$ (I*b*), 99%
(I*c*)	Orange	Scarlet ppt. $\xrightarrow{\text{alkali}}$ (I*c*), 100%
(I*d*)	Olive-green	Dark red ppt. $\xrightarrow{\text{alkali}}$ (I*d*), 98%
(I*e*)	Deep yellow	Orange ppt., changing to phthalimide (32%) in 30 min.
(I*a*)	Orange	Orange ppt., changing to phthalimide in 15 min.

The macrocycles also combined with acetic acid but the products were not stable to heat. Thus the benzene macrocycle (I*b*) formed an orange crystalline product with 3 mols. of acetic acid, from which the macrocycle was regenerated at 155°, and the acridine macrocycle (I*d*) yielded a red diacetate trihydrate, which lost acetic acid at 210°. The naphthalene macrocycle formed an orange-coloured compound (apparently non-stoicheiometric) which lost acetic acid at 180°. It seems that these products are crystal solvates rather than salts of acetic acid. The yellow product from the 3 : 5-pyridine macrocycle (I*e*), however, which contains 2 mols. of combined acetic acid, is probably a dipyridinium diacetate.

Quaternisation of the macrocycles with methyl iodide was also examined. As previously mentioned (*J.*, 1952, 5008), the 2 : 6-pyridine macrocycle (I*a*) failed to react at 100°. The 3 : 5-pyridine macrocycle (I*e*), on the other hand, easily formed a (sparingly soluble) dimethiodide. Acid hydrolysis of this and treatment of the hydrolysate with picric acid afforded in good yield 3 : 5-diamino-1-methylpyridinium picrate. Quaternisation of the macrocycle (I*e*) had therefore occurred on the pyridine-nitrogen atoms : these, being situated on the periphery of the great ring system in the molecule, are accessible to the reagent. Surprisingly, the benzene and the naphthalene macrocycles (I*b* and *c*) formed dimethiodides : these were insoluble and infusible. It seems likely in these derivatives that quaternisation has been effected on two of the four nitrogen atoms which provide the aza-links; one of the possible bond structures is shown in formula (II).

Attempted degradation of the dimethiodides of the benzene and the naphthalene macrocycle (II*b* and *c*) by acid hydrolysis unfortunately produced intractable tars. With warm aqueous sodium hydroxide, however, the orange-red benzene macrocycle dimethiodide (II*b*) yielded a yellow solid, which was readily soluble in methanol, unlike the parent macrocycle or its salts. Crystals of the product rapidly effloresced in the air and afforded the (sparingly soluble) parent benzene macrocycle (I*b*). The new (soluble) product was not merely a methanol solvate of the macrocycle, however : it was evidently the dimethohydroxide corresponding to (II*b*). This was shown by the following results. Treatment of the product with hydrogen iodide regenerated the dimethiodide (II*b*). The benzene macrocycle hydriodide, prepared for comparison, differed in being maroon-coloured, and in giving back the macrocycle instantly with alkali. Moreover, an authentic dimethanol solvate of the benzene macrocycle was obtained by keeping the macrocycle under methanol for several days. It formed yellow needles, which did not effloresce and were only sparingly soluble in methanol.

The highly insoluble crimson naphthalene macrocycle dimethiodide (II*c*) reacted with

aqueous alkali only very slowly even at the boiling point, to regenerate the naphthalene macrocycle (I*c*) (presumably *via* an unstable quaternary hydroxide).

Under the conditions previously employed, methylation of the acridine macrocycle was incomplete, and the dark product contained only 1·6 mols. of combined methyl iodide. It was hydrolysed cleanly in boiling hydrochloric acid, and an orange chloride was isolated. This has not been identified and the position of methylation of the acridine macrocycle remains uncertain.

Of the cross-conjugated macrocycles which we have so far described, only the 2 : 6-pyridine macrocycle (I*a*) has a central structural arrangement akin to that in the porphyrins and azaporphins. As was expected, therefore, only this compound of the present series formed analogous complexes with one equivalent of bivalent metals (*J.*, 1952, 5008). No metal-containing derivatives could be obtained from the benzene, naphthalene, and acridine macrocycles. Incidental to the experiments, a crystal solvate of the last macrocycle was encountered, which contained 2 mols. each of formamide and water. However,

TABLE 3. *Ultra-violet light absorption characteristics of macrocycles and related linear compounds.*

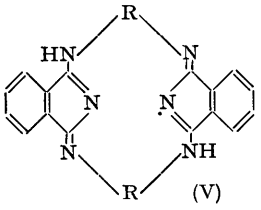
Macrocycle (I) (in H·CO·NMe_2)	$\lambda_{max.}$ (Å)	ε	Compound (IV) (in EtOH) †	$\lambda_{max.}$ (Å)	ε
b	2800	25,000	(i) R′ = Ph, R″ = H	2510	12,200
	3280	17,100		2560	
	3430			2640	
				3030	8,900
				3280	
				3480	7,700
				3650	6,500
c	2800	44,200	(ii) *B*, R′ = Ph, R″ = Me	2580	11,200
	3050	32,400	(see p. 2494)	2680	12,400
	3150	27,500		2810	
	3350	29,100		2900	
	3520	32,400		3680	14,600
	3620	31,800			
d	2800	58,900	(iii) R′ = 2-naphthyl, R″ = H	2270	63,500
	3240	46,000		2340	
	3360	53,100		3260	9,100
	3630	46,000		3600	10,750
e	2800	27,800	(iv) R′ = 3-pyridyl, R″ = H	2350	29,900
	2900			2510	14,300
	3150	19,800		2660	12,500
	3300	22,900		2800	
				2900	
				3040	
				3150	
				3530	10,700
a	2800	*	(v) R′ = 2-pyridyl, R″ = H	2310	31,300
	2900			2740	19,800
	3240			2840 ‡	18,500
	3430			3300	16,900
				3450	18,300
				3640	20,500
				3830	21,800

* The solution is too dilute for accurate intensity measurements (*J.*, 1952, 5008).
† From *J.*, 1953, 3593; 1952, 5000. ‡ Inflexion.

the 3 : 5-pyridine macrocycle (I*e*) with copper and zinc acetates in dimethylformamide yielded a brown copper derivative, $C_{30}H_{28}O_7N_8Cu_2$, and a yellow zinc derivative, $C_{30}H_{28}O_7N_8Zn_2$. The empirical formulæ showed that 2 atoms of metal were combined with one macrocycle residue, together with acetate residues and water, thus: $C_{30}H_{28}O_7N_8M_2$ is made up of $C_{26}H_{16}N_8 + 2OAc + 3H_2O + 2M$. The derivatives were amorphous, insoluble, infusible, and very stable thermally. Consequently we suggest that these metal derivatives have macromolecular extended-lattice structures. Certainly they are not complexes of the normal porphyrin or azaporphin type, which indeed are not to be expected.

The light absorptions of the macrocycles (I) are given in Table 3, which includes, for comparison, the data for the related linear 3-unit compounds (IV). The spectra of the macrocycles accord with the cross-conjugated structures. They show that the macrocycles have no chromophores additional to the chromophoric systems present in the corresponding linear 3-unit compounds (IV). There can be no contribution to the structures from (conceivable) tautomers in which there is a fully conjugated great ring, in the way that is evident for the nickel derivative of the 2 : 6-pyridine macrocycle, as mentioned already.

It was concluded previously (*J.*, 1953, 3593) that the linear compounds (IV; R″ = H) were capable of tautomerism. Members of the series appeared to exist in solution either in the di-imino*iso*indoline form (IV*A*) or the aminoimino*iso*indolenine form (IV*B*), or as mixtures. A characteristic of compounds with the fixed structure (IV*B*), *e.g.* (ii) (Table 3), was absorption of light in the 3680—3790 Å region, whilst the structure (*A*) appeared not to show absorption maxima beyond about 3200 Å. It was concluded that the diphenyl derivative (i) (Table 3) was a tautomeric mixture of the two forms in solution. In the dinaphthyl compound (iii), it appeared that the *iso*indolenine form (*B*) predominated. We can add that the di-3-pyridyl compound (iv) appears to be a mixture, whilst the di-2-pyridyl isomer (v) probably exists entirely in the form (*B*), in ethanol.



(V)

By making comparisons, we can tentatively assign fine structures to the macrocycles. The benzene and the two pyridine macrocycles do not absorb light at such long wave-lengths as the corresponding linear compounds. We suggest therefore (from Table 3) that these three macrocycles (in dimethylformamide) correspond predominately to the type (*A*) structure, and are probably best represented by the formulæ (I*b*, *e*, and *a*). In the naphthalene and the acridine macrocycle there appears to be a greater contribution from form (*B*) structures, so that the alternative representations (V*c* and *d*) seem more appropriate.

The hydrochlorides (and methiodides) of the benzene, naphthalene, and acridine macrocycles are more deeply coloured than the parent compounds. Because of their insolubility it was not possible to determine by ultra-violet absorption methods whether the salts had structures analogous in type to that proposed for the hydrochloride of diphenylimino*iso*indoline (*J.*, 1953, 3593). This hydrochloride in acetic acid showed an absorption maximum at 3980 Å (ε 20,000). However, we were able to make measurements on solutions of some of the bases in concentrated sulphuric acid. The spectra (see Table 4) are simpler than those observed for other solvents and show very broad maxima. It may

TABLE 4. *Light absorptions in concentrated sulphuric acid.*

Compound	$\lambda_{max.}$ (Å)	ε	Compound	$\lambda_{max.}$ (Å)	ε
(I*b*	2445	55,900	(I*c*)	2435	84,000
	3605	27,500		3690	33,400
		(4,800 at 4000 Å)			(21,800 at 4000 Å
					3,400 at 4900 Å)
(IV; R′ = Ph, R″ = H)	2375	28,300			
	3695	14,700			
		(9,600 at 4000 Å)			

be concluded that the benzene and the naphthalene macrocycle, and diphenylimino*iso*indoline, have analogous structures in sulphuric acid solution. The common chromophore appears to be that of aminoimino*iso*indolenine (IV*B*), which doubtless is doubly protonated; the preparation (in the absence of water) of a dihydrochloride of di-imino*iso*indoline (*J.*, 1952, 5000) shows this to be feasible.

EXPERIMENTAL

Preparation of the Macrocycles.—(i) *The benzene macrocycle* (I*b*). 1 : 3-Di-imino*iso*indoline (13·6 g.) and *m*-phenylenediamine (10 g.; purified) were heated together in boiling ethanol (or butanol) (200 c.c.) for 17 hr., during which ammonia was evolved. After being washed with

ethanol, the yellow solid (15·7 g., 71%) had m. p. 375°. From nitrobenzene, the benzene *macrocycle* (I*b*) crystallised as very small yellow needles, m. p. 380°; sublimation in nitrogen at 340°/15 mm. gave needles several mm. long [Found: C, 76·8; H, 4·2; N, 19·0%; *M* (ebullioscopic in nitrobenzene), 380, 472, 407. $C_{28}H_{18}N_6$ requires C, 76·7; H, 4·1; N, 19·2%; *M*, 438].

(ii) *The naphthalene macrocycle* (I*c*). Similarly, the di-imine (9·2 g.) was heated with 2 : 7-diaminonaphthalene (10 g.) in boiling ethanol (or butanol) (100 c.c.), and the yellow product (14 g., 82%) washed well with ethanol. Several extractive crystallisations (Soxhlet) with pyridine, and sublimation at 400—450°/15 mm., afforded fine yellow needles, m. p. *ca.* 500° (decomp.), of the naphthalene *macrocycle* (I*c*) [Found: C, 80·35; H, 4·1; N, 15·5%; *M* (ebullioscopic in nitrobenzene), 561, 532. $C_{36}H_{22}N_6$ requires C, 80·3; H, 4·1; N, 15·6%; *M*, 538].

(iii) *The acridine macrocycle* (I*d*). From the di-imine (5·8 g.) and 2 : 8-diaminoacridine (8·36 g.) in boiling butanol (100 c.c.), ammonia was evolved and a brown product (8·5 g.) separated. After being washed with butanol and ether, and extractively crystallised (Soxhlet) several times from pyridine, the acridine *macrocycle* (I*d*) formed deep-yellow rods with a bronze lustre (2·4 g., 18%), which gradually decomposed at >400° (Found: C, 78·6; H, 4·2; N, 17·6. $C_{42}H_{24}N_8$ requires C, 78·7; H, 3·8; N, 17·5%).

(iv) *The* 3 : 5-*pyridine macrocycle* (I*e*). A solution of the di-imine (1·5 g.) and 3 : 5-diaminopyridine (1 g.) in butanol (20 c.c.) was boiled for 17 hr. (ammonia evolved) and then cooled. Crystallisation of the solid (1·88 g.) from nitrobenzene afforded the 3 : 5-pyridine *macrocycle* (I*d*) (925 mg., 46%) as very small yellow needles, m. p. 436° (decomp.) (Found: C, 70·7; H, 3·9; N, 25·9. $C_{26}H_{16}N_8$ requires C, 70·9; H, 3·7; N, 25·5%).

Hydrolysis of the Macrocycles.—(i) The benzene macrocycle (I*b*) (0·1 g.) was recovered after being boiled with a mixture of concentrated hydrochloric acid (10 c.c.) and glacial acetic acid (10 c.c.) for 2 hr. When the benzene macrocycle (0·5 g.), concentrated hydrochloric acid (10 c.c.) and acetic acid (10 c.c.) were heated together at 150° for 7 hr. and the solution cooled, phthalic acid separated [0·23 g.; m. p. 196—197° (decomp.)]. The filtrate was evaporated to dryness, and the residue taken up in cold water (3 c.c.), undissolved phthalic acid (0·13 g.) being collected (total yield of phthalic acid, 0·36 g., 1·90 mols.; *S*-benzylthiuronium salt, m. p. and mixed m. p. 158—159°). The filtrate was added to picric acid (0·65 g.) in water (65 c.c.), the mixture was chilled in ice, and the *m*-phenylenediamine picrate collected, washed with water, and dried [yield, 0·69 g., 1·79 mols.; m. p. and mixed m. p. 181° (decomp.)].

(ii) The naphthalene macrocycle (0·5 g.) was not hydrolysed by a mixture of concentrated hydrochloric acid (10 c.c.) and acetic acid (10 c.c.) at 150° for 4 hr.; heating at 180° for 15 hr. was necessary for the degradation. The dark solution was evaporated to dryness and the residue warmed with N-sodium hydroxide (10 c.c.) for 10 min., during which ammonia was evolved. The mixture was cooled in ice, and 2 : 7-diaminonaphthalene (0·27 g., 1·84 mols.) collected [picrate, m. p. and mixed m. p. 209° (decomp.)]. Acidification of the filtrate with concentrated hydrochloric acid caused precipitation of phthalic acid [0·26 g., 1·68 mols., m. p. 195—196° (decomp.); *S*-benzylthiuronium salt, m. p. and mixed m. p. 158°].

(iii) The acridine macrocycle (I*d*) (220 mg.) was boiled with concentrated hydrochloric acid (10 c.c.) for *ca.* 15 min. The solution was evaporated to dryness, the residue warmed with 2N-sodium hydroxide (10 c.c.), the 2 : 8-diaminoacridine was collected [139 mg., 1·93 mols.; m p. and mixed m. p. (sealed tube) 275°], and the filtrate evaporated to small bulk and acidified with concentrated hydrochloric acid. Phthalic acid separated [93 mg., 1·63 mols., m. p. 191° (decomp.); *S*-benzylthiuronium salt, m. p. and mixed m. p. 158—159°].

(iv) The 3 : 5-pyridine macrocycle (205 mg.) was heated under reflux with 2N-hydrochloric acid (10 c.c.) for *ca.* 30 min., and the solution was filtered from a trace of a dark material, and evaporated to dryness. Trituration of the residue with water (2 c.c.) afforded phthalic acid (138 mg., 1·78 mols.), m. p. 195° (decomp.); *S*-benzylthiuronium salt, m. p. and mixed m. p. 159°. A further portion of the macrocycle (223 mg.) was similarly hydrolysed and the solution evaporated. Excess of aqueous sodium hydroxide was added and, by continuous extraction of the solution with benzene, 3 : 5-diaminopyridine (90·5 mg., 1·64 mols.) was isolated, m. p. and mixed m. p. 112—113°.

Hydrochlorides of the Macrocycles.—(i) Addition of ethanolic hydrogen chloride to a solution of the benzene macrocycle (200 mg.) in ethanol (200 c.c.) caused precipitation of the infusible orange-red *dihydrochloride* (220 mg., 94%), which was collected and washed with ethanol by centrifugation (Found: Cl, 12·8. $C_{28}H_{20}N_6Cl_2$ requires Cl, 13·9%). Treatment with sodium hydroxide regenerated the macrocycle, m. p. and mixed m. p. 380°.

(ii) Similarly from the naphthalene macrocycle in dioxan, the scarlet *dihydrochloride* was obtained (Found: Cl, 11·5. $C_{36}H_{24}N_6Cl_2$ requires Cl, 11·6%), from which sodium hydroxide regenerated the yellow macrocycle, m. p. *ca.* 500° (decomp.).

(iii) Trituration of the acridine macrocycle (53 mg.) with concentrated hydrochloric acid (5 c.c.) for 5 min. gave a dark hydrochloride (60 mg.), which was washed with concentrated hydrochloric acid, methanol, and ether [Found, after being dried (*a*) at 10^{-5} mm. for 8 hr. and (*b*) at 200°/10^{-4} mm. for 3 hr.: Cl, (*a*) 12·85, (*b*) 7·4. Calc. for $C_{42}H_{27}N_8Cl_3$: Cl, 14·2. Calc. for $C_{42}H_{26}N_8Cl_2$: Cl, 9·9%].

(iv) When the 3 : 5-pyridine macrocycle (70 mg.) was stirred with 2N-hydrochloric acid for 5 min., the salmon-pink *dihydrochloride* (76 mg.) separated (Found: Cl, 13·7. $C_{26}H_{18}N_8Cl_2$ requires Cl, 13·8%).

Compounds of the Macrocycles with Acetic Acid.—(i) The benzene macrocycle (291 mg.) was dissolved in boiling glacial acetic acid (15 c.c.), and the red solution evaporated to 5 c.c. The *triacetate* (381 mg.) separated as orange rhombs, which were dried at 10^{-6} mm. for 3 hr. (Found: C, 65·7; H, 5·3; N, 14·0. $C_{28}H_{18}N_6,3C_2H_4O_2$ requires C, 66·0; H, 4·9; N, 13·6%). The compound lost acetic acid at 155° and reverted to the macrocycle.

(ii) When boiled with acetic acid (20 c.c.) for 30 min., the naphthalene macrocycle (102·5 mg.) was converted into an orange product (159 mg.) (Found: C, 69·1; H, 5·05; N, 13·8. Calc. for $C_{36}H_{22}N_6,2C_2H_4O_2$: C, 72·9; H, 4·6; N, 12·8. Calc. for $C_{36}H_{22}N_6,C_2H_4O_2,3H_2O$: C, 69·9; H, 4·9; N, 12·9%), which lost acetic acid at 175—180°.

(iii) A solution of the acridine macrocycle (144 mg.) in boiling acetic acid (15 c.c.) deposited a red *triacetate dihydrate* (Found: C, 66·5; H, 5·1; N, 13·8. $C_{42}H_{24}N_8,3C_2H_4O_2,2H_2O$ requires C, 67·3; H, 4·7; N, 13·1%).

(iv) The 3 : 5-pyridine macrocycle (33 mg.) was dissolved in hot acetic acid (5 c.c.), and the filtered solution evaporated to 1 c.c. Orange crystals (26 mg.) of the *diacetate* slowly separated (Found, after being dried over KOH: C, 63·7; H, 4·4; N, 20·5. $C_{26}H_{16}N_8,2C_2H_4O_2$ requires C, 64·3; H, 4·3; N, 20·0%).

Compounds of the Macrocycles with Methyl Iodide.—(a) *Preparations.* The 3 : 5-pyridine macrocycle was heated with a large excess of purified methyl iodide in a sealed glass tube (air removed) at 100° for 24 hr. The *dimethiodide* was an orange infusible powder (Found: I, 34·65. $C_{28}H_{22}N_8I_2$ requires I, 35·0%).

Similarly obtained were the orange-red benzene macrocycle *dimethiodide* (Found: I, 36·8. $C_{30}H_{24}N_6I_2$ requires I, 35·1%), the crimson naphthalene macrocycle *dimethiodide* (Found: I, 29·9. $C_{38}H_{28}N_6I_2$ requires I, 30·85%), and a dark product from the acridine macrocycle (Found: I, 22·2. Calc. for $C_{42}H_{24}N_8,2MeI$: I, 27·45%).

(b) *Hydrolyses.* (i) The 3 : 5-pyridine macrocycle dimethiodide (295 mg.) was warmed with 2N-hydrochloric acid (10 c.c.) on the steam-bath until hydrolysis was complete. The solution was then evaporated, and a filtered aqueous extract (3 c.c.) of the residue was treated with an excess of aqueous picric acid. 3 : 5-Diamino-1-methylpyridinium picrate (250 mg., 1·74 mols.) separated, m. p. 200—201° after recrystallisation from water. The m. p. was not depressed by authentic material, described below.

(ii) The acridine macrocycle methiodide (341 mg.) was boiled with 15% aqueous hydrochloric acid for 1 hr., and the red solution was filtered and cooled. The orange product (a hydrochloride) (276 mg.), after several crystallisations from 15% hydrochloric acid, had m. p. >360° (Found: C, 53·3; H, 5·5; H, 14·35%). Light absorption in ethanol: max. at 2630, 2800, 4600 Å (ε 1650, 780, 1300). Acriflavine, recrystallised similarly, formed orange-red crystals, m. p. *ca.* 255° (decomp.). Light absorption in EtOH (at same concentration as preceding substance): max. at 2620, 2820, 4650 Å (ε 1980, 820, 1700). 2 : 8-Diaminoacridine hydrochloride crystallised from 15% hydrochloric acid as a very dark brown microcrystalline powder, m. p. >300°.

(c) *Action of alkali.* (i) A suspension of the benzene macrocycle dimethiodide (544 mg.) in 2N-sodium hydroxide (10 c.c.) was warmed until the solid had become yellow. The methohydroxide was collected and washed with water. The filtrate and washings were treated with 2N-nitric acid and an excess of aqueous silver nitrate, whereupon silver iodide was precipitated (387 mg., 2·18 mols.). The yellow methohydroxide dissolved easily in methanol, and on concentration of the solution yellow needles separated, having m. p. 360—361°; these effloresced rapidly in the air to a yellow methanol-insoluble powder, m. p. 380° undepressed by the parent benzene macrocycle. Addition of iodine-free hydriodic acid to a methanolic solution of the methohydroxide caused precipitation of the orange dimethiodide (identified by its behaviour with alkali). The benzene macrocycle *dihydriodide* was a maroon-coloured powder, m. p.

>500° (Found: I, 33·6. $C_{28}H_{20}N_6I_2$ requires I, 36·6%), which with 2N-sodium hydroxide at once gave the benzene macrocycle, m. p. and mixed m. p. 379°. When kept under methanol for several days, the benzene macrocycle was transformed into beautiful yellow needles of the sparingly soluble *dimethanol* solvate which was stable in the air; when a portion (92·8 mg.) was heated at 100°/0·1 mm. for 1 hr., it lost the solvent (Found: loss in wt., 10·5. $C_{28}H_{18}N_6$,2MeOH requires MeOH, 12·7%) and gave back the macrocycle (84·0 mg.).

(ii) Treatment of the naphthalene macrocycle dimethiodide (817 mg.) with boiling 2N-sodium hydroxide (10 c.c.) slowly gave a yellow solid (530 mg.), m. p. *ca.* 500°, indistinguishable from the parent naphthalene macrocycle. From the filtrate, silver iodide was precipitated (313 mg., 1·34 mols.).

Attempted Preparation of Metal Derivatives of the Macrocycles.—(i) Hot solutions of the benzene macrocycle (127 mg.) and cobalt acetate (77 mg.) in dimethylformamide (3-c.c. portions) were mixed. After evaporation of the solvent, and washing of the residue with methanol, unchanged macrocycle (117 mg.) was recovered, m. p. 380°. Similar results were obtained with nickel, copper, and zinc acetate. The naphthalene macrocycle likewise failed to yield a metal derivative.

(ii) A solution of the acridine macrocycle (14·8 mg.) in hot dimethylformamide (20 c.c.), treated with cobalt acetate (25·7 mg.) or copper or nickel acetate in the same solvent (2 c.c.), and then cooled, deposited orange crystals (12 mg.) of the *solvated* acridine macrocycle (metal-free borax bead), also obtained in the absence of metal salts (Found: C, 70·5; H, 5·1; N, 16·6. $C_{42}H_{24}N_8$,2H·CO·NMe_2,2H_2O requires C, 70·0; H, 5·1; N, 17·0%). The solvate evolved liquid and became lighter in colour at 150°, the residue decomposing at >400°. When heated at 200°/0·1 mm. for 2 hr., the solvate (63·6 mg.) was reconverted into the acridine macrocycle (49·3 mg., 1 mol.) (Found: N, 17·2. Calc. for $C_{42}H_{24}N_8$: N, 17·5%).

(iii) Mixing of solutions of the 3 : 5-pyridine macrocycle (65·7 mg.) and copper acetate (62·7 mg.) in dimethylformamide (5-c.c. portions) caused precipitation of a brown, amorphous, infusible *copper* complex (54·3 mg.) (Found: C, 48·9; H, 4·0; N, 15·5; Cu, 18·0. $C_{30}H_{28}O_7N_8Cu_2$ requires C, 48·7; H, 3·8; N, 15·2; Cu, 17·2%).

Addition of zinc acetate (61 mg.) in dimethylformamide (0·5 c.c.) to the 3 : 5-pyridine macrocycle (53 mg.) in the same solvent (3 c.c.) gave, during 24 hr., a yellow amorphous precipitate of the *zinc* complex (90·8 mg.) (Found: C, 48·5; H, 3·8; N, 13·9, 14·0; Zn, 17·5. $C_{30}H_{28}O_7N_8Zn_2$ requires C, 48·5; H, 3·8; N, 15·1; Zn, 17·6%).

3 : 5-*Diamino*-1-*methylpyridinium Picrate.*—3 : 5-Diaminopyridine (0·1 g.) was warmed with an excess of methyl iodide for 5 min., and the solution evaporated. The residue was taken up in ethanol (10 c.c.) and ethanolic picric acid added. 3 : 5-*Diamino*-1-*methylpyridinium picrate* crystallised from water and had m. p. 201° (decomp.) (Found: C, 40·9; H, 3·9; N, 23·75. $C_{12}H_{12}O_7N_6$ requires C, 40·9; H, 3·4; N, 23·9%).

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DEPARTMENT OF ORGANIC CHEMISTRY, IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY, SOUTH KENSINGTON, LONDON, S.W.7. [*Received, March 20th*, 1954.]