139. *Heterocyclic Imines and Amines. Part VIII.* Identification of "o-Cyanothiobenzamide" as 1-Imino-3-thioisoindoline, and its Conversion with Amines into Macrocycles and Intermediates.*

By M. E. Baguley and J. A. Elvidge.

The primary product from phthalonitrile and hydrogen sulphide is not *o*-cyanothiobenzamide [1] (II) but is 1-imino-3-thio*iso*indoline (III). This is established by reactions and by infrared and ultraviolet absorption spectroscopy. The fine structure of the compound is discussed.

Condensation of (III) and its *S*-methyl derivative (VIII) with aromatic and aliphatic amines has been studied briefly. Reaction can occur at one or both of the exocyclic functional groups of (III) and (VIII), whilst, with butylamine, (III) gives 2-butyl-1-butylimino-3-thio*iso*indoline (XVII), both the cyclic and the exocyclic imino-group having been displaced. With *m*-phenylenediamine and 2 : 6-diaminopyridine, 3-unit products (XXV) and (XXVI) are obtainable. Their conversion into cross-conjugated macrocycles has been examined.

The addition of 1 mol. of hydrogen sulphide to phthalonitrile (I) has been reported by Drew and Kelly [1] to give *o*-cyanothiobenzamide (II). We have found that this structure is incorrect: the product is actually an isomeric, heterocyclic compound, 1-imino-3-thio-*iso*indoline (III).[2] Recently, workers at Farbenfabriken Bayer A.G. have stated this without giving details.[3] We therefore present our evidence and discuss the fine structure

* Part VII, *J.*, 1956, 4135.

[1] Drew and Kelly, *J.*, 1941, 630 (cf. Porter, Robinson, and Wyler, *ibid.*, p. 620).
[2] Baguley, Ph.D. Thesis, London, 1955.
[3] Baumann, Bienert, Rösch, Vollmann, and Wolf, *Angew. Chem.*, 1956, **68**, 133.

of the compound. We have also examined briefly its potentialities for the preparation of macrocycles and their intermediates.

The addition of hydrogen sulphide to phthalonitrile in the presence of sodium hydrogen sulphide gives, as described,[1] mainly a compound $C_8H_6N_2S$, together with some dithio-β-*iso*indigo from a concomitant bimolecular reduction. In the original reports [1] no conclusive evidence for the structure (II) for the primary product was presented. Drew and Kelly recorded that hydrolysis with aqueous acid gave monothiophthalimide (IV), *via* a presumed transient cyclic intermediate (III), and that hydrogen chloride added readily in boiling benzene to yield a product which was arbitrarily assigned the imino-chloride structure (V).

It seemed to us that structure (V) was improbable. The hydrogen chloride product was more likely to be the hydrochloride of the cyclic base (III), particularly as in the oxygen series *o*-cyanobenzamide (VI) with hydrogen chloride gives the hydrochloride of the imino-imide (VII).[4] Indeed, treatment of the sulphur-containing hydrogen chloride product, $C_8H_7N_2ClS,H_2O$, with sodium carbonate or even water gave a base. Now this was identical with the primary compound from phthalonitrile and hydrogen sulphide, which meant that the compound very probably had the cyclic structure (III) and was not *o*-cyanothiobenzamide (II).

Structure (III) accommodated well the mild hydrolysis to monothiophthalimide (IV). Moreover, mild oxidation with hydrogen peroxide and alkali gave iminophthalimide (VII), as was then expected, whilst methyl iodide and alkali yielded an *S*-methyl derivative (VIII) which was readily hydrolysed by aqueous acid to phthalimide (IX).

Further structural evidence came from light-absorption measurements.

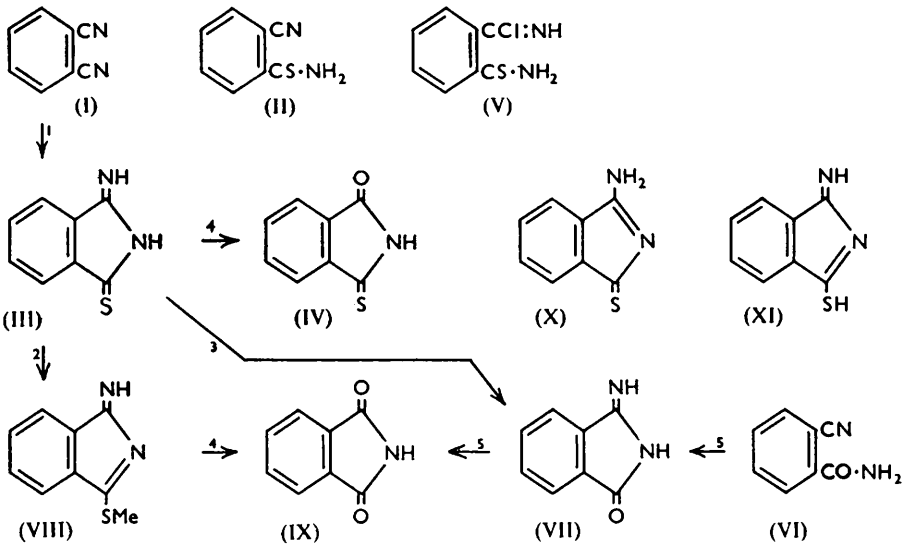
In the infrared spectrum, the compound (in Nujol mull and in potassium bromide disc) shows no C≡N stretching vibration. Strong absorption near 1664 cm.$^{-1}$ indicates C=N stretching, and a single intense band at 3135 cm.$^{-1}$ indicates N–H stretching in a secondary amino-group. The necessarily fixed-bond, *S*-methyl derivative has these same characteristics with C≡N again absent. The parent compound and the derivative must therefore have the cyclic structures (III) and (VIII). A medium-intensity band near 1582 cm.$^{-1}$ in the spectrum of (III), which is absent from that of the *S*-methyl derivative (VIII), can be attributed [5] to the *N*-substituted thioamide grouping –NH–C=S. Hence in the solid state, the potentially tautomeric molecule (III) exists in that bond form and not appreciably in the amino-form (X). There may be a small concentration of the thiol form (XI) present because there is very weak absorption at 2681 cm.$^{-1}$.

The ultraviolet absorption data afforded full support. Because the replacement of an oxygen by a sulphur auxochromic group in many chromophores results in a bathochromic shift of the pertinent ultraviolet absorption maximum by 450—500 Å (with an increase in ε),[6] the light absorptions of sulphur analogues can often be predicted from the data for the oxygen-containing compounds. Thus, as the imino-imide (VII) has a longest-wavelength absorption maximum at 2920 Å,[7] the sulphur analogue (III) would be expected to have a maximum at roughly 3400 Å. On the other hand, from the data for benzonitrile [8] and thiobenzamide (max. at 2650, 3700 Å),[9] the acyclic *o*-cyanothiobenzamide structure (II) would be expected to show absorption maxima at about 2700 and 3700 Å. In fact, the phthalonitrile–hydrogen sulphide product has an absorption maximum at 3450 Å, which clearly points to the structure (III). The iminothio*iso*indoline form (III) evidently predominates in ethanol solution because the light absorption (Table) is similar to that for the fixed structure (XVII) (see below). The *S*-methyl derivative (VIII), which has a

[4] Elvidge and Linstead, *J.*, 1952, 5000.
[5] Randall, Fowler, Fuson, and Dangl, "Infrared Determination of Organic Structures," Van Nostrand Co., New York, 1949; Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co., Ltd., London, 1954.
[6] Braude, *Ann. Reports*, 1945, **42**, 105.
[7] Clark, Elvidge, and Linstead, *J.*, 1953, 3593.
[8] Scheibe, *Ber.*, 1926, **59**, 2617.

fixed imino-thio*iso*indolenine structure, has a very weak absorption maximum at the much longer wavelength of 4360 Å.

Hence the phthalonitrile–hydrogen sulphide product, $C_8H_6N_2S$, is undoubtedly cyclic and evidently exists predominantly in the form (III) in the solid state and in ethanol



Reagents: 1, H_2S. 2, MeI—OH^-. 3, H_2O_2—OH^-. 4, Aq. HCl. 5, See ref. 4.

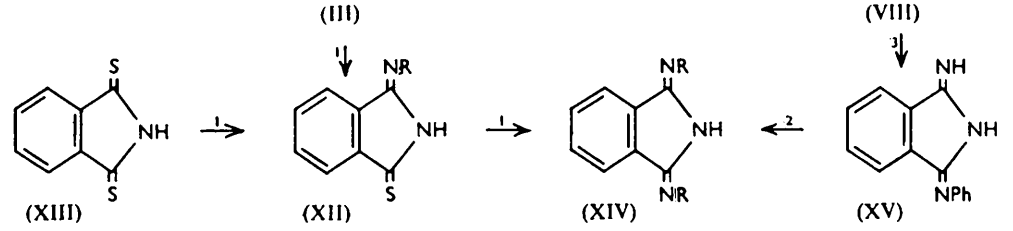
solution. Removal of a proton (by alkali) would be expected to yield an anion derived from the thiol form (XI), which would undergo methylation at the position of highest electron density: as expected, the product is the *S*-methyl derivative (VIII).

Condensations.—Imidines have two reactive exocyclic functional groups and they can condense readily with 2 mols. of many an amine [4, 7, 10, 11, 12] but comparatively few stepwise reactions have been achieved.[7, 10, 12] The *iso*indole derivatives (III) and (VIII) have two reactive, but different, exocyclic functional groups, so the possibility of effecting step-wise condensations with these compounds appeared good. The hoped-for 2- and 3-unit products were required in connection with studies of macrocycle formation.[13, 14, 15]

Drew and Kelly [1] observed that the compound (III) condensed with aniline under mild conditions, to give 1-phenylimino-3-thio*iso*indoline (XII; R = Ph), the imino-group reacting and being eliminated as ammonia. This we have confirmed. With 2-amino-pyridine, the analogous compound (XII; R = 2-C_5H_4N) was formed: its nature was confirmed by a preparation from dithiophthalimide (XIII) and 1 mol. of aminopyridine (this proceeded with elimination of hydrogen sulphide and was accompanied by a bimolecular reduction with formation of dithio-β-*iso*indigo). With 2 mols. of aniline and of 2-aminopyridine in boiling ethanol, compound (III) reacted at both functional groups to furnish the known disubstituted imidines [4, 7] (XIV; R = Ph and 2-C_5H_4N). The *S*-methyl derivative (VIII) did not react cleanly with 2-aminopyridine, butylamine, or morpholine, but with aniline at room temperature it gave the monophenyl-imidine (XV).[7] Thus the *S*-methyl derivative (VIII) reacted preferentially at the sulphur functional group in contrast to the compound (III).

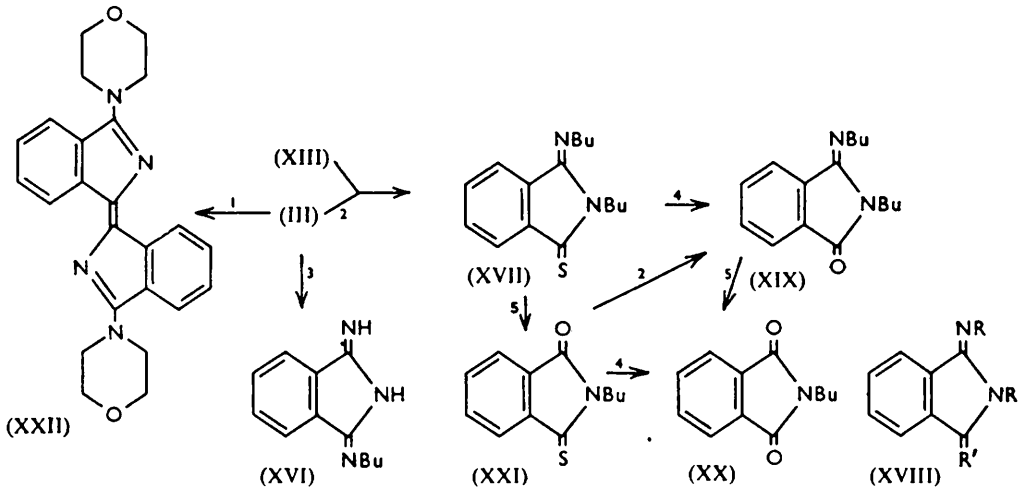
[9] Burawoy, *Ber.*, 1931, **64**, 462.
[10] Elvidge and Linstead, *J.*, 1954, 442.
[11] Ficken and Linstead, *J.*, 1955, 3525; Linstead and Whalley, *ibid.*, p. 3530.
[12] Clark, Elvidge, and Golden, *J.*, 1956, 4135.
[13] Clark, Elvidge, and Linstead, *J.*, 1954, 2490.
[14] Elvidge and Linstead, *J.*, 1955, 3536.
[15] Elvidge and Golden, preceding paper.

With primary aliphatic amines, the iminothio*iso*indoline (III) underwent an unexpected reaction. Whereas in the presence of aqueous sodium hydroxide it reacted with butylamine to give the known monobutylimidine [7] (XVI) with elimination of the elements of hydrogen sulphide, alone with butylamine in boiling ethanol it afforded a dibutyl derivative, $C_{16}H_{22}N_2S$, with elimination of ammonia. The structure (XVII) for this product was indicated by the reactions shown. Benzylamine similarly yielded a dibenzylated product, given the structure (XVIII; R = CH_2Ph, R′ = S) by analogy. Oxidation of



Reagents: 1, NH_2R. 2, NH_2Ph, R = Ph. 3, NH_2Ph.

the dibutyl derivative with alkaline hydrogen peroxide gave a compound $C_{16}H_{22}ON_2$. This was evidently the dibutyl oxo-compound (XIX) because the light absorption closely resembled that of the known dimethyl derivative [12] (XVIII; R = Me, R′ = O) and hydrolysis yielded *N*-butylphthalimide (XX). Acid hydrolysis of the product (XVII) caused replacement of a BuN: residue by O: so that the product was formulated as *N*-butylmonothiophthalimide (XXI). In agreement, this degradation product underwent oxidation to *N*-butylphthalimide (XX), and it condensed with butylamine to yield the previously encountered dibutyl-oxo-compound (XIX) with elimination of hydrogen sulphide.



Reagents: 1, Morpholine. 2, NH_2Bu. 3, NH_2Bu–OH^-. 4, H_2O_2–OH^-. 5, H_2O–H^+.

The dibutyl-thio*iso*indoline (XVII) was also obtained by condensation of dithiophthalimide (XIII) with butylamine, but the major reaction here was a bimolecular reductive coupling to dithio-β-*iso*indigo. With morpholine, the iminothio*iso*indoline (III) yielded mainly di-(3-morpholino-1-*iso*indolinylidene) (XXII), previously prepared [16] by condensing dithio-β-*iso*indigo with morpholine.

Attention was then turned to condensations with *m*-phenylenediamine and 2 : 6-diaminopyridine.

[16] Elvidge and Golden, *J.*, 1956, 4144.

Mixtures of the iminothio*iso*indoline (III) with *m*-phenylenediamine in the molar ratios 1 : 2, 1 : 1, and 2 : 1 when heated in boiling benzene afforded the benzene macrocycle (XXIII) as sole identified product. Thus both of the exocyclic functional groups of (III) were reactive towards the diamine. With 2 : 6-diaminopyridine, however, the 2-unit product (XXIV) was obtained, condensation having occurred at the imino-group, as with aniline (above).

1-Imino-3-methylthio*iso*indolenine (VIII), on the other hand, reacted preferentially and readily at the sulphur group. Thus with *m*-phenylenediamine it condensed twice, with elimination of 2 mols. of methanethiol per diamine unit, to yield the benzene 3-unit product (XXV). With 2 : 6-diaminopyridine, it yielded the pyridine 3-unit product (XXVI). The products (XXV) and (XXVI) separated with water of crystallisation, which was removed by drying at 130°/10^{-4} mm. Both were hydrolysed easily by aqueous hydrochloric acid to 2 mols. of phthalimide which confirmed the structures. An analogous 3-unit compound derived from 2 : 4-diaminotoluene has already been described.[15]

These 3-unit compounds have a longest-wavelength absorption maximum in the 3400—3460 Å region, so they resemble the corresponding cross-conjugated macrocycles. Thus the benzene 3-unit compound (XXV) (see Table) has a maximum at 3460 Å with ε 9100,

Light absorptions in ethanol.

Compound	$\lambda_{max.}$ (Å)	ε	Compound	$\lambda_{max.}$ (Å)	ε	Compound	$\lambda_{max.}$ (Å)	ε
(III)	2340	19,400	(XVII)	3000	9,800	(XXV), anhydrous	2260	65,500
	3100	13,500		3480	12,900		2550	31,300
	3450	7,900					3050	12,700
			(XIX)	2520	15,500		3460	9,100
(VIII)	2850	9,500		3020	4,500			
	4360	530				(XXVI), monohydrate	2340	48,000
			(XVIII; R = Me, R′ = O) (in MeOH)	2500[12]	14,300		2700	23,000
(XIII)[19]	2280	7,500		2980	3,500		3400	38,000
	2400	13,000						
	2600	5,300						
	3800	18,800						

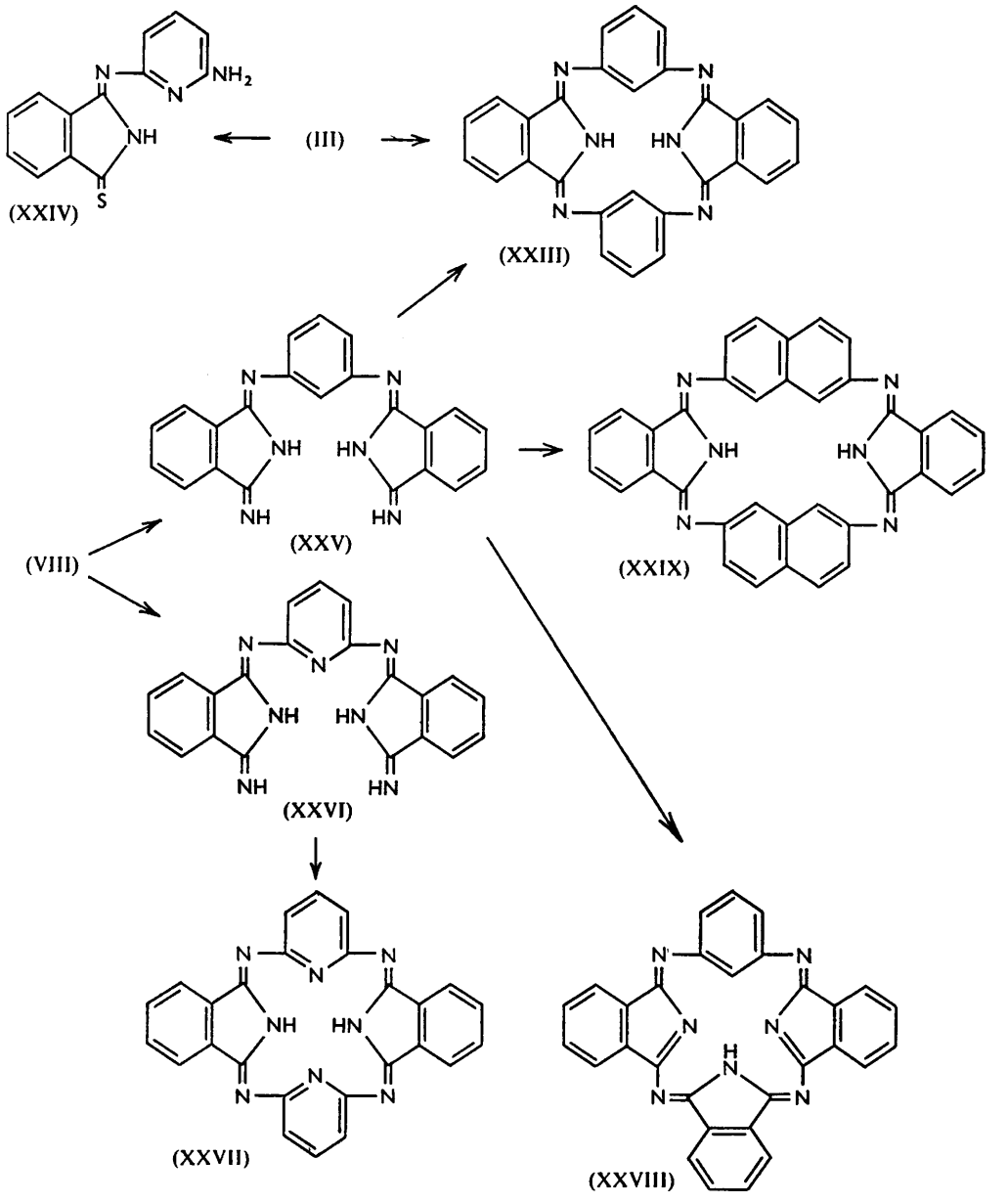
whilst the benzene macrocycle (XXIII) has $\lambda_{max.}$ 3430[13] or 3340 Å[15] (depending on solvent) with ε 17,000—19,000; this indicates that they contain the same effective chromophore, which presumably approximates to (XXX), and that this is electronically isolated from the rest of the molecule in each case. There are two of these groupings in the molecule of the macrocycle (XXIII) and this absorbs with twice the intensity of the open-chain compound (XXV). Similar remarks apply to the 2 : 4-toluene 3-unit compound and macrocycle described previously,[15] but data for the 2 : 6-pyridine compounds are as yet incomplete.

The possibility of effecting macrocyclic ring syntheses from the 3-unit compounds (XXV) and (XXVI) received attention.

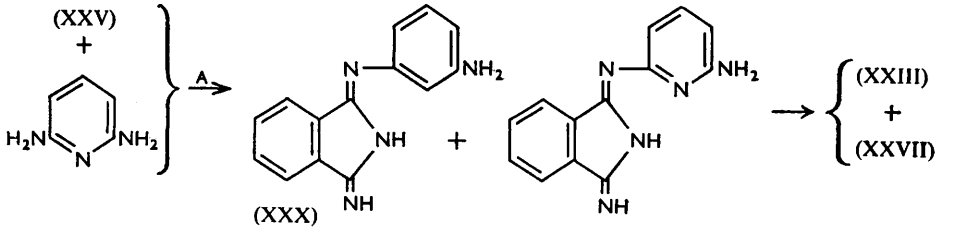
Heating the benzene 3-unit compound (XXV) in ethanol with *m*-phenylenediamine afforded the yellow benzene macrocycle[13] (XXIII). The pyridine compound (XXVI) was less reactive and was unchanged after being heated similarly with 2 : 6-diaminopyridine, but in boiling butanol condensation occurred with formation of the orange 2 : 6-pyridine macrocycle[17] (XXVII). A third straight-forward condensation was that between the 3-unit benzene compound (XXV) and 1 mol. of di-imino*iso*indoline, which gave the burgundy-red tri*iso*indole-benzene macrocycle[15] (XXVIII).

The last reaction suggested that other unsymmetrical cross-conjugated macrocycles might be obtained by analogous ring-closures of the 3-unit intermediates (XXV) and (XXVI). The attempts were unsuccessful however. Thus the less reactive pyridine 3-unit compound (XXVI) was recovered after being heated with di-imino*iso*indoline in boiling ethanol or butanol. Interaction of (XXVI) with *m*-phenylenediamine, however,

[17] Elvidge and Linstead, *J.*, 1952, 5008.

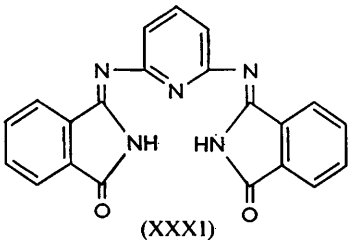


gave a mixture from which only the 2 : 6-pyridine macrocycle (XXVII) was isolated (as its nickel derivative).[17] The alternative condensation between the benzene 3-unit



compound (XXV) and 2 : 6-diaminopyridine yielded the benzene macrocycle (XXIII), together with the 2 : 6-pyridine macrocycle (XXVII), which was again isolated as the much less soluble nickel derivative. From the condensation of the benzene 3-unit product (XXV) with 2 : 7-diaminonaphthalene, the symmetrical naphthalene macrocycle [13] (XXIX) was obtained in high yield.

These results indicated that the 3-unit compounds (XXV) and (XXVI) have rather unreactive terminal functional groups. The failures to yield unsymmetrical macrocycles by condensation, *e.g.*, with favourably orientated diamines, and the formation instead of symmetrical macrocycles is significant. Evidently the 3-unit compounds are split by amines, and the resulting 2-unit products undergo self-condensations rather than interaction so that symmetrical macrocycles are the main products. The reaction A recalls the interchange reactions of *N*-substituted amidines with amines,[18] and the displacement reactions of amines with *N*-substituted imidines,[12] a particularly close analogy being the reaction between the 3-unit compound (XXXI) and 2 : 6-diaminopyridine.[4]



(XXXI)

Discussion of the fine structures of the 3-unit intermediates, *e.g.*, (XXV), and the macrocycles is deferred until more data on fixed-bond structures have been accumulated.

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 Spectrographic Laboratory of this Department.

1-*Imino*-3-*thio*isoindoline (III).—(a) *Preparation.* Drew and Kelly's method [1] (for "*o*-cyanothiobenzamide") was slightly modified in that a fine suspension of phthalonitrile in ethanol was stirred for 9 hr. with aqueous sodium hydrogen sulphide which had previously been saturated with hydrogen sulphide. Addition of water precipitated a first crop of the product (37%), decomp. from 195°, whilst addition to the filtrate of 2N-hydrochloric acid almost to neutrality afforded less pure material (24%). Recrystallisation of the first crop from ethanol gave golden needles of 1-*imino*-3-*thio*iso*indoline* (70% recovery) which softened and decomposed at 218° (Found : C, 59·7; H, 3·95; N, 17·7. $C_8H_6N_2S$ requires C, 59·3; H, 3·7; N, 17·3%). Principal infrared max. : (i) KBr disc, 3135, 2681, 1664, 1582, 1466, 1385, 1289, 1271, 1239, 1214, 1079, 905, 766, 671 cm.$^{-1}$; (ii) Nujol mull, 3135, 2681, 1661, 1577, 1287, 1267, 1239, 1211, 1078, 903, 764, 670 cm.$^{-1}$.

Porter, Robinson, and Wyler's similar method [1] afforded the same product contaminated with sparingly soluble dithio-β-*iso*indigo ($\lambda_{max.}$ 4760, 5080 Å) (see below).

(b) *Hydrolysis.* When 1-imino-3-thio*iso*indoline (200 mg.) was heated on the steam-bath with 2N-hydrochloric acid (5 c.c.) a red solution was obtained, which shortly deposited solid. After 4 min., the mixture was cooled and filtered, and a second crop was collected 5 hr. later. The red needles (112 mg., 62%) had m. p. 176—177° and mixed m. p. 177° with monothiophthalimide, m. p. 177°. Porter, Robinson, and Wyler [1] give m. p. 175°.

(c) *Hydrochloride.* (i) 1-Imino-3-thio*iso*indoline was boiled in benzene for 1 hr. whilst dry hydrogen chloride was passed in (cf. ref. 1). The pink solid did not melt below 300°. On being washed with aqueous sodium carbonate, the solid became yellow-brown and it then had a decomp. pt. *ca.* 218°, alone and mixed with 1-imino-3-thio*iso*indoline. (ii) Treatment of 1-imino-3-thio*iso*indoline in ethanol with ethanolic hydrogen chloride at 0°, and concentration of the solution to a very small bulk, gave 1-imino-3-thio*iso*indoline *hydrochloride hydrate* as needles which softened at *ca.* 165° but did not melt below 300° (Found : C, 44·3; H, 4·5; Cl, 16·7. $C_8H_7N_2ClS,H_2O$ requires C, 44·3; H, 4·2; Cl, 16·4%). This salt (100 mg.) was added to water (5 c.c.). The solid became yellowish-brown and a part dissolved to a yellow solution which almost at once deposited fine golden needles. The solid (70 mg., 93%) decomposed at

[18] Roberts, *J. Amer. Chem. Soc.*, 1950, **72**, 3603; Roberts, DeWolfe, and Ross, *ibid.*, 1951, **73**, 2277.

ca. 218° alone and mixed with 1-imino-3-thio*iso*indoline. Drying of the hydrated salt in a vacuum desiccator gave the anhydrous *hydrochloride*, m.p. >300° (Found: C, 48·15; H, 3·7. $C_8H_7N_2SCl$ requires C, 48·4; H, 3·55%).

(d) *Oxidation.* (i) 30% Hydrogen peroxide (4·5 c.c.) was added in portions during 30 min. to a cooled, stirred solution of 1-imino-3-thio*iso*indoline (1·6 g.) in 2N-sodium hydroxide (10 c.c.) and ethanol (15 c.c.). After 12 hr., the solution was evaporated under reduced pressure and the residue extracted with ethanol. 1-Imino-3-oxo*iso*indoline (0·22 g., 15%) was isolated. having m. p. 198° and mixed m. p. 202°. (ii) The solution from a similar oxidation was concentrated to 25 c.c., acidified with hydrochloric acid, and heated on the steam-bath for 10 min. Cooling the solution caused the separation of phthalimide (0·72 g., 50%), m. p. and mixed m. p. 234°.

1-*Imino*-3-*methylthio*iso*indolenine* (VIII).—(a) *Preparation.* A solution of 1-imino-3-thio*iso*indoline (8·1 g.) in ethanol (75 c.c.) and 2N-sodium hydroxide (25 c.c., 1 equiv.) was diluted with water (75 c.c.), and then cooled to 0° and stirred whilst dimethyl sulphate (15 c.c.; freshly distilled) was added in drops during 5 min. After a further 5 min., water (200 c.c.) was added. The 1-*imino*-3-*methylthio*iso*indolenine* (6·8 g., 77%) crystallised from aqueous ethanol as needles, m. p. 98—100° (Found: C, 61·3; H, 4·9; N, 15·6; S, 17·9. $C_9H_8N_2S$ requires C, 61·35; H, 4·6; N, 15·9; S, 18·2%). Principal infrared max.: Nujol mull, 3135, 1653, 1323, 1267, 1242, 1155, 1048, 963, 764, 681 cm.$^{-1}$.

(b) *Hydrolysis.* The derivative (50 mg.) was warmed with 2N-hydrochloric acid (2 c.c.) for several minutes. Methanethiol was evolved, and from the cooled solution phthalimide separated (30 mg., 72%), m. p. and mixed m. p. 230—232°.

Condensations with Arylmonoamines.—1-Imino-3-thio*iso*indoline (0·32 g.) was boiled in ethanol (50 c.c.) with aniline (0·18 g., 1 mol.) for 12 hr. Evaporation of the solution, extraction of tar from the residue with boiling light petroleum (b. p. 60—80°), and trituration of the residue with ethanol provided 1-phenylimino-3-thio*iso*indoline (XII; R = Ph) (0·2 g., 43%), m. p. 205—208°, which crystallised from ethanol as orange-yellow needles, m. p. 209° (Found: C, 70·8; H, 4·8. Calc. for $C_{14}H_{10}N_2S$: C, 70·5; H, 4·2%). Drew and Kelly [1] reported m. p. 209°.

Interaction of 1-imino-3-thio*iso*indoline (4 g.) with 2-aminopyridine (4·7 g.) in boiling ethanol (200 c.c.) for 24 hr. and concentration of the solution gave 1-2′-pyridylimino-3-thio*iso*indoline (XII; R = 2-C_5H_4N) which crystallised from ethanol (charcoal) as orange-brown needles (2·3 g., 39%), m. p. 175° and mixed m. p. 175—178° with the compound next prepared.

Dithiophthalimide [19] (XIII) (0·89 g.) was added in portions (*ca.* 25 mg.) to a boiling solution of 2-aminopyridine (0·47 g., 1 mol.) in ethanol (25 c.c.) during 3 hr. After a further hour's boiling, the hot mixture was filtered from dithio-β-*iso*indigo (0·09 g.). When cooled, the filtrate deposited 1-2′-*pyridylimino*-3-*thio*iso*indoline* (0·53 g., 38%), which crystallised from ethanol as orange-brown needles, m. p. 178° (Found: C, 64·9; H, 3·8; N, 18·0; S, 13·3. $C_{13}H_9N_3S$ requires C, 65·2; H, 3·8; N, 17·6; S, 13·4%).

1-Imino-3-thio*iso*indoline (0·32 g.) and aniline (0·37 g., 2 mols.) were boiled in ethanol (50 c.c.) until evolution of ammonia ceased (12 hr.). Evaporation of the solution afforded a residue completely soluble in boiling light petroleum (b. p. 60—80°). Concentration and cooling of this solution gave 1 : 3-diphenylimino*iso*indoline [7] (XIV; R = Ph) as yellow needles (0·55 g., 93%), m. p. 122—123° and mixed m. p. 126—128°.

1-Imino-3-thio*iso*indoline (0·32 g.) and 2-aminopyridine (0·37 g., 2 mols.) were boiled in butanol (20 c.c.) for 4 hr., and the solution was then evaporated. Crystallisation of the residue from ethanol (charcoal) afforded 1 : 3-di-2′-pyridylimino*iso*indoline [4] (XIV; R = 2-C_5H_4N) (0·24 g., 41%) as pale yellow needles, m. p. and mixed m. p. 165—170°.

1-Imino-3-methylthio*iso*indolenine (VIII) (0·35 g.) and aniline (0·18 g., 1 mol.) were kept together in methanol (3 c.c.) for 24 hr. The precipitate crystallised from methanol as yellow needles (0·25 g., 60%), m. p. 202—204° (decomp.) alone and mixed with 1-imino-3-phenylimino*iso*indoline [7] (XV).

Condensation Products from Alkylmonoamines.—(a) 3-*Butylimino*-1-*imino*iso*indoline* (XVI). 1-Imino-3-thio*iso*indoline (1·6 g.) in 2N-sodium hydroxide (75 c.c.) was treated with butylamine (0·73 g.) in ethanol (10 c.c.). After several hours, an oil had separated, which solidified at 0°. From benzene, the 3-butylimino-1-imino*iso*indoline (0·7 g., 35%) separated as needles, m. p. and mixed m. p. 162—163° (decomp.).[7]

[19] Drew and Kelly, *J.*, 1941, 625.

(b) 2-*Butyl*-1-*butylimino*-3-*thio*isoindoline (XVII). 1-Imino-3-thioisoindoline (4·05 g.) and butylamine (9 c.c., 4 mols.) were boiled in methanol (65 c.c.) for 3 hr. and the solution was then evaporated to 25 c.c. 2-*Butyl*-1-*butylimino*-3-*thio*isoindoline (2·6 g., 31%) crystallised (m. p. 58—58·5°), and was recrystallised from methanol to give yellow needles, m. p. 61° (Found: C, 70·3; H, 8·2; N, 10·4. $C_{16}H_{22}N_2S$ requires C, 70·0; H, 8·1; N, 10·2%).

To the compound (XVII) (2 g.) in methanol (50 c.c.) containing potassium hydroxide (0·82 g., 2 equiv.), kept at *ca.* 50°, 30% hydrogen peroxide was added in portions of 1—2 c.c. until the solution became neutral. The almost colourless solution was concentrated under reduced pressure to 25 c.c. and then water was added to produce a turbidity. At 0° overnight, pale yellow crystals separated. Several crystallisations from aqueous methanol provided colourless laths of 2-*butyl*-1-*butylimino*-3-*oxo*isoindoline (XIX), m. p. 33·5—34° (corr.) (Found: 74·3; H, 8·7; N, 11·1. $C_{16}H_{22}ON_2$ requires C, 74·4; H, 8·6; N, 10·85%). Hydrolysis of the 2-butyl-1-butylimino-3-oxoisoindoline (1 g.) with boiling 2N-hydrochloric acid (15 c.c.) for 25 minutes afforded an oil (0·5 g., 64%), which had b. p. 308° (Emich). After being distilled under reduced pressure and kept at 0°, the oil solidified and then had m. p. 30—31° undepressed by *N*-butylphthalimide.

2-Butyl-1-butylimino-3-thioisoindoline (8·5 g.) was boiled with 2N-hydrochloric acid (100 c.c.) for 10 min. The mixture was extracted with chloroform (30 c.c.), and the extract was dried (Na_2SO_4) and distilled, finally under reduced pressure, to give a red oil (5 g.), b. p. 102—103°/0·1 mm., n_D^{15} 1·6294, which soon solidified. From light petroleum (b. p. 40—60°), the 2-*butyl*-1-*oxo*-3-*thio*isoindoline (XXI) formed elongated prisms, m. p. 29—29·5° (corr.) (Found: C, 65·3; H, 6·0; N, 6·3. $C_{12}H_{13}ONS$ requires C, 65·7; H, 6·0; N, 6·4%). Oxidation of this product (4·0 g.) in methanol (60 c.c.) containing dissolved potassium hydroxide (1·9 g., 2 equivs.) was effected at 50—60°, by 30% hydrogen peroxide added in 1—2 c.c. portions until the solution became neutral. The filtrate from potassium sulphate was evaporated and the residue distilled under reduced pressure. The *N*-butylphthalimide (1·5 g., 40%), b. p. 188—190°/28 mm., n_D^{31} 1·5410, b. p. 308—309° (Emich), solidified at 0° and then had m. p. and mixed m. p. 31—32°. Previous workers recorded b. p. 311·8°/758 mm.[20] and m. p. 32°[21] and 34°.[22]

2-Butyl-1-oxo-3-thioisoindoline (2·35 g.) was boiled in ethanol (30 c.c.) with butylamine (2 c.c.) until evolution of hydrogen sulphide ceased (*ca.* 2 hr.). The solution was evaporated and the residue chromatographed in benzene on alumina (Spence, type H). A pale yellow band was washed off the column, which was then eluted with benzene containing 5% of ethanol. Evaporation of the latter eluate and crystallisation of the residue from methanol afforded laths, m. p. 32—33° undepressed by 2-butyl-1-butylimino-3-oxoisoindoline.

Dithiophthalimide [19] (0·74 g.) and butylamine (0·36 g., 1 mol.) were boiled in ethanol (20 c.c.) for 1 hr. Filtration of the hot solution gave dithio-β-*iso*indigo (0·36 g., 59%), $\lambda_{max.}$ in ethanol at 4760, 5080 Å (visual determination). [With I. S. Fox. Dithio-β-*iso*indigo [19] in ethanol has $\lambda_{max.}$ 2320, 3190, 3380, 3530, 4760, and 5080 Å with $10^{-3}\varepsilon$ 21·3, 10·8, 10·8, 10·4, 35·7, and 46·2 respectively.] Concentration of the filtrate afforded yellow needles of 2-butyl-1-butylimino-3-thioisoindoline (0·17 g., 15%), m. p. and mixed m. p. 58°.

(c) 2-*Benzyl*-1-*benzylimino*-3-*thio*isoindoline (XVIII; R = CH_2Ph, R′ = S). 1-Imino-3-thioisoindoline (1·6 g.) and benzylamine (2·14 g.) were boiled together in methanol (50 c.c.) for 15 min. The solution was filtered through charcoal, concentrated to 25 c.c. and cooled. Recrystallisation of the precipitate from methanol afforded an unidentified solid, m. p. 205°, and, from the mother-liquors, 2-*benzyl*-1-*benzylimino*-3-*thio*isoindoline (1·3 g., 38%) as yellowish needles, m. p. 108° (Found: N, 8·1. $C_{22}H_{18}N_2S$ requires N, 8·2%).

(d) *Di*-(3-*morpholino*-1-iso*indolinylidene*) (XXII). 1-Imino-3-thioisoindoline (3·24 g.) and morpholine (4 c.c.) were boiled in methanol (100 c.c.) for 24 hr. and the hot mixture was filtered. The solid was washed with 2N-sodium hydroxide–ethanol (1 : 1) until the washings were colourless. The remaining solid crystallised from dioxan as orange needles (1·1 g., 27%) and was identified as di-(3-morpholino-1-*iso*indolinylidene) [16] by mixed m. p. (Found: C, 72·4; H, 5·5. Calc. for $C_{24}H_{24}O_2N_4$: C, 72·0; H, 6·0%).

Condensations with m-*Phenylenediamine and* 2 : 6-*Diaminopyridine*.—1-Imino-3-thioisoindoline (1·6 g.) and *m*-phenylenediamine (1·1 g., 1 mol.) were boiled in ethanol (50 c.c.) for 2 hr. The mixture was cooled and the brownish solid crystallised from ethanol (charcoal) several

[20] Sachs, *Ber.*, 1898, **31**, 1225.
[21] Horák and Novotny, *Chem. Listy*, 1952, **46**, 357.
[22] Vanags, *Acta Univ. Latviensis, Kim. Fakultat*, 1939, Ser. 4, No. 8, 405.

times, giving the yellow benzene macrocycle (XXIII) (0·5 g., 23%), m. p. and mixed m. p. 368—372°.

1-Imino-3-thio*iso*indoline (3·2 g.) and 2 : 6-diaminopyridine (4·3 g.) were boiled in ethanol (50 c.c.) for 6 hr. Filtration of the boiling mixture through charcoal, and cooling of the filtrate afforded 1-(2-*amino*-6-*pyridylimino*)-3-*thio*iso*indoline* (XXIV) which separated from nitrobenzene as a deep orange microcrystalline powder (2·3 g., 41%), m. p. 243° (Found: C, 61·0; H, 4·1. $C_{13}H_{10}N_4S$ requires C, 61·4; H, 4·0%).

1-Imino-3-methylthio*iso*indolenine (3·5 g.) and *m*-phenylenediamine (1·08 g., 0·5 mol.) were kept in chloroform (25 c.c.) for 48 hr. Crystallistion of the precipitate from methanol gave yellow prisms of m-*di*-(1-*imino*-3-iso*indolinylideneamino*)*benzene* (XXV) *trihydrate* (1·7 g., 21%), m. p. 268° (decomp.) (Found: C, 63·3; H, 5·2. $C_{22}H_{16}N_6,3H_2O$ requires C, 63·1; H, 5·3%), which was converted at 100°/10^{-5} mm. into the anhydrous *compound*, m. p. unchanged (Found: 72·1; H, 4·6; N, 22·8. $C_{22}H_{16}N_6$ requires C, 72·5; H, 4·4; N, 23·1%) (cf. ref. 15). Evaporation of the chloroform reaction liquors and crystallisation of the residue from methanol yielded the benzene macrocycle, m. p. 373—374° and mixed m. p. 374—375°.[13] *m*-Di-(1-imino-3-*iso*indolinylideneamino)benzene (0·76 g.) was boiled with 2N-hydrochloric acid (3 c.c.) for 5 min. and the mixture then cooled in ice. Phthalimide separated (0·56 g., 1·82 mols.), m. p. and mixed m. p. 234—236°.

A solution of 1-imino-3-methylthio*iso*indolenine (1·76 g.) and 2 : 6-diaminopyridine (0·54 g., 0·5 mol.) in chloroform (25 c.c.) was kept for 48 hr. and then evaporated. The residue was triturated with methanol. Crystallisation from methanol afforded orange 2 : 6-*di*-(1-*imino*-3-iso*indolinylideneamino*)*pyridine* (XXVI) *hydrate* (0·59 g., 31%), m. p. 243° (decomp.) (Found: C, 65·5; H, 4·4; N, 25·5. $C_{21}H_{15}N_7,H_2O$ requires C, 65·8; H, 4·5; N, 25·6%). Drying at 130°/10^{-4} mm. for 2 hr. reduced the water content to that of a *hemihydrate*, m. p. unchanged (Found: C, 67·4; H, 4·5. $C_{21}H_{15}N_7,\frac{1}{2}H_2O$ requires C, 67·35; H, 4·3%). The hydrate (0·305 g.) was warmed with 2N-hydrochloric acid (2 c.c.) on the steam-bath for 5 min., and the mixture then cooled in ice. The solid was phthalimide (0·22 g., 1·88 mols.), m. p. and mixed m. p. 234—237°.

Macrocycles from the 3-*Unit Compounds* (XXV) *and* (XXVI).—Compound (XXV) (0·3 g.) and *m*-phenylenediamine (0·1 g.) were boiled in ethanol (25 c.c.) overnight, and the solution was then cooled. The yellow benzene macrocycle (XXIII) separated (40%), having m. p. 368—370° and mixed m. p. 370—372°.[13]

Compound (XXV) (0·36 g.) and 2 : 6-diaminopyridine (0·11 g.) were boiled in butanol (15 c.c.) for 4 hr. The solution was evaporated somewhat and cooled, and the product crystallised from nitrobenzene, giving the orange 2 : 6-pyridine macrocycle (XXVII) (0·16 g., 38%) with m. p. and mixed m. p. 336—338°.[17]

Compound (XXV) (0·18 g.) and di-imino*iso*indoline (0·1 g.) were boiled in ethanol (25 c.c.) for 12 hr. A rapid crystallisation of the dark red solid from nitrobenzene gave tri*iso*indole-benzene macrocycle (XXVIII) as burgundy-red needles (0·11 g., 49%), m. p. 356—360° and mixed m. p. 358—361°.[15]

Compound (XXVI) (0·73 g.) and *m*-phenylenediamine (0·22 g., 1 mol.) were boiled in butanol (20 c.c.) for 4 hr. The solvent was removed under reduced pressure and the residue dissolved in very hot nitrobenzene (30 c.c.). Nickel acetate (0·5 g.) in a minimum of formamide was added, the mixture was cooled, and the crystalline precipitate collected. From nitrobenzene, brown needles of the nickel derivative of the 2 : 6-pyridine macrocycle (XXVII) separated (0·45 g.); they had m. p. and mixed m. p. 364—366°.[17] Evaporation of the reaction liquors afforded tar.

Compound (XXV) (0·67 g.) and 2 : 6-diaminopyridine (0·22 g., 1 mol.) were boiled in butanol (50 c.c.) for 4 hr. Next day, the mixture of products was collected dissolved in boiling nitrobenzene, and treated with nickel acetate (250 mg.) in formamide. The brown needles (0·31 g.) had m. p. 350—352°, and, after recrystallisation from nitrobenzene, m. p. 365° not depressed by the nickel derivative of the 2 : 6-pyridine macrocycle (XXVII). The reaction liquors were evaporated, and the residue was washed with light petroleum (b. p. 60—80°) and heated with boiling 2N-hydrochloric acid (25 c.c.) for 10 min. to hydrolyse intermediates and any remaining pyridine macrocycle. The boiling mixture was filtered, and the yellow solid was washed with hot water, dried, and crystallised from benzene. Yellow laths of benzene macrocycle (XXIII) (0·17 g.), m. p. and mixed m. p. 370—374°, separated.

Compound (XXV) (0·73 g.) and 2 : 7-diaminonaphthalene (0·4 g.) were boiled in ethanol

(50 c.c.) for 24 hr. The yellow product (0·59 g.) was naphthalene macrocycle (XXIX),[13] m. p. and mixed m. p. 510° (decomp.).

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