799. *Heterocyclic Imines and Amines. Part VII.** N-*Substituted Phthalic Imidine Derivatives and their Reactions with Amines.*†

By P. F. Clark, J. A. Elvidge, and J. H. Golden.

The condensation reactions of some *N*-substituted derivatives of di-imino-*iso*indoline with amines have been examined. In some cases there is direct replacement of the exocyclic imino-functions by the amine (as shown in *a*, below) but in other cases rearrangements are encountered (of the type *b*).

Structures have been determined, and light absorptions are given and discussed.

N-Methyl and other derivatives (I) of the imidine of phthalic acid have been prepared, and a preliminary examination has been made of their condensation reactions with primary amines. Two types of reaction have been encountered. In some cases there is a direct replacement of one or both of the exocyclic substituents, as indicated in the abbreviated reaction schemes *a* (i) and (ii). In other cases there is a rearrangement consequent upon the interaction, as indicated in *b* (i). Condensation with rearrangement has also been encountered with unsubstituted imidines: the overall reaction is then as in *b* (ii).

Three routes were used for the preparation of the imidine derivatives (I), *viz.*, condensation of amines with di-imino*iso*indoline,[1] alkylation of the imidine or its derivatives,[2] and the addition of amines to phthalonitrile.[2,3] For some of the required compounds, only one of the routes succeeded.

The structures of the new compounds were determined by mild hydrolysis with hydrochloric acid, a method which has proved reliable hitherto.[2,3,4] Compounds of the types (I; R′ = H) ‡ yield phthalimide whilst a compound of the type (I*A*; R′ ≠ H) yields an *N*-substituted phthalimide.

Preparations.—Di-imino*iso*indoline (I; R = R′ = R″ = H) with methyl iodide at 80° gave a lemon-yellow salt, $C_9H_{10}N_3I$. This was evidently the hydriodide of the 3-methyl derivative (I; R = Me, R′ = R″ = H) because hydrolysis yielded phthalimide and not *N*-methylphthalimide. From di-imino*iso*indoline and from phthalonitrile, with methylamine at 100°, 1 : 3-dimethylimino*iso*indoline (I; R = R″ = Me, R′ = H) was obtained: this base had one active hydrogen atom, gave a picrate and a hydrochloride, and on hydrolysis afforded phthalimide *via* the 3-methylimino-1-oxo-derivative (II; R = Me,

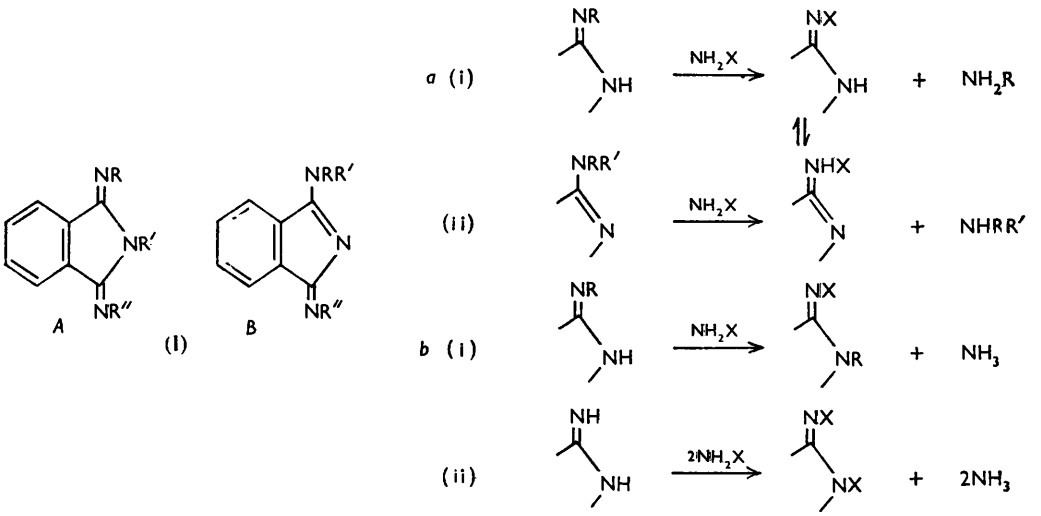
* Part VI, *J.*, 1956, 235.

† Submitted in honour of the seventieth birthday of Sir Ian Heilbron, D.S.O., F.R.S.

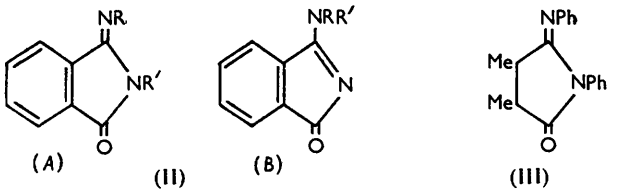
‡ The omission of *A* and *B* in the formula designation indicates that the compound is potentially tautomeric.

[1] Elvidge and Linstead, *J.*, 1952, 5000.
[2] Clark, Elvidge, and Linstead, *J.*, 1953, 3593.
[3] Elvidge and Linstead, *J.*, 1954, 442.
[4] Linstead and Whalley, *J.*, 1955, 3530.

R′ = H) which was isolated as the sparingly soluble hydrochloride. More vigorous treatment of di-imino*iso*indoline or 1 : 3-dimethylimino*iso*indoline with methylamine did not effect further methylation but gave a β-*iso*indigo compound.[5] However, a trimethyl derivative was obtained, as its yellow hydriodide, $C_{11}H_{14}N_3I$, from 1 : 3-dimethylimino*iso*indoline and methyl iodide at 100°. The trimethyl derivative yielded phthalimide on hydrolysis, which indicated the structure (I*B*; R = R′ = R″ = Me).



In parallel experiments, the imino-imide (II; R = R′ = H) was found to condense with 2 mols. of methylamine, rather than 1 mol. as expected from previous work.[1] The product, which gave *N*-methylphthalimide on hydrolysis, was necessarily the 2-methyl-3-methylimino-compound (II*A*; R = R′ = Me). Its formation was reminiscent of the



production of the derivative (III) from dimethylsuccinimidine and aniline hydrochloride.[4] Both reactions are examples of the type *b* (ii) condensation which must involve a rearrangement. With ethanolic solutions of *m*-aminoacetanilide and of piperidine, the imino-imide (II; R = R′ = H) yielded the " normal " derivatives (II; R = *m*-C_6H_4·NHAc, R′ = H) and (II*B*; RR′ = ·$[CH_2]_5$·), each of which gave phthalimide on hydrolysis. With aqueous-ethanolic ethylamine, however, there was hydrolysis of the imino-imide ring and formation of *NN*′-diethylphthalamide.

Attempts to obtain the unsymmetrical dimethyl derivative (I*B*; R = R′ = Me, R″ = H) by condensation of di-imino*iso*indoline with dimethylamine, or by addition of dimethylamine to phthalonitrile, failed. The only tractable product was phthalocyanine, which suggested that the required derivative was highly reactive. However, diethylamine was successfully added to phthalonitrile, and the very labile product, presumed to be the base (I*B*; R = R′ = Et, R″ = H), was isolated as the picrate. A similar labile base was obtained from morpholine and phthalonitrile. This was isolated as the hemihydrate and

[5] Elvidge and Golden, following paper.

characterised as the picrate. That the base had the cyclic structure (I*B*; RR′ = ·$[CH_2]_2$·O·$[CH_2]_2$·, R″ = H) was indicated by its hydrolysis with cold water to imino-phthalimide (II; R = R′ = H) in good yield, a result which also demonstrated that the substituted amino-function was the more reactive of the two exocyclic nitrogen groups. Further work on compounds of this type is in progress.

The symmetrical 1 : 3-diethyl derivative (I; R = R″ = Et, R′ = H), which yielded phthalimide on hydrolysis, was obtained by the addition of ethylamine to phthalonitrile. 1 : 3-Dibenzyliminoisoindoline (I; R = R″ = CH_2Ph, R′ = H) was obtained by the alternative method, condensation of benzylamine in ethanol with di-iminoisoindoline : the product gave phthalimide on hydrolysis, as expected. Similarly prepared was 1 : 3-di-*m*-acetamidophenyliminoisoindoline, which crystallised as a stable hemihydrate. This disubstitution product was accompanied by a small quantity of the monosubstituted imidine, 3-*m*-acetamidophenylimino-1-iminoisoindoline (I; R = *m*-C_6H_4·NHAc, R′ = R″ = H), further reaction of which with *m*-aminoacetanilide gave the dicondensation product. Hydrolyses confirmed the structures.

Condensations.—The foregoing morpholino- and diethylamino-imines (I*B*; R″ = H, RR′ = ·$[CH_2]_2$·O·$[CH_2]_2$· and Et_2) soon became red or greenish-blue at ordinary temperature. Above 100°, alone or in solution, they rapidly decomposed with formation of phthalocyanine. This contrasted with the stability of di-iminoisoindoline itself, which gave phthalocyanine in appreciable yields only at elevated temperature in the presence of hydrogen donors.[6] For comparison, portions of the morpholino-imine were heated in boiling tetralin and in nitrobenzene : 33% yields of phthalocyanine were obtained within a few minutes, irrespective of whether the solvent was a hydrogen donor or dehydrogenating agent (cf. ref. 6).

With aniline in the cold, the morpholino- and the diethylamino-imine afforded the known monophenylimidine [2] (I; R = Ph, R′ = R″ = H) by a ready replacement of the substituted amino-group, and there was no production of ammonia. Treatment of the imines (I*B*; R″ = H, RR′ = ·$[CH_2]_2$·O·$[CH_2]_2$· and Et_2) with boiling butylamine rapidly afforded 1 : 3-dibutyliminoisoindoline [2] (I; R = R″ = Bu, R′ = H), both substituted and unsubstituted exocyclic nitrogen functions being replaced : in this reaction, therefore, ammonia was evolved. In extension, it was shown that 3-morpholino-1-oxoisoindolenine [2] (II*B*; RR′ = ·$[CH_2]_2$·O·$[CH_2]_2$·) with aniline in boiling ethanol gave the phenyl analogue (II; R = Ph, R′ = H), that the monophenyl-imidine (I; R = Ph, R′ = R″ = H) with an excess of boiling butylamine yielded 1 : 3-dibutyliminoisoindoline (I; R = R″ = Bu, R′ = H), and that 1 : 3-dimethyliminoisoindoline with 2-aminopyridine yielded the 1 : 3-dipyridyl-imidine [1] (IV) with evolution of methylamine. These several reactions are examples of the type *a* direct-displacement condensations.

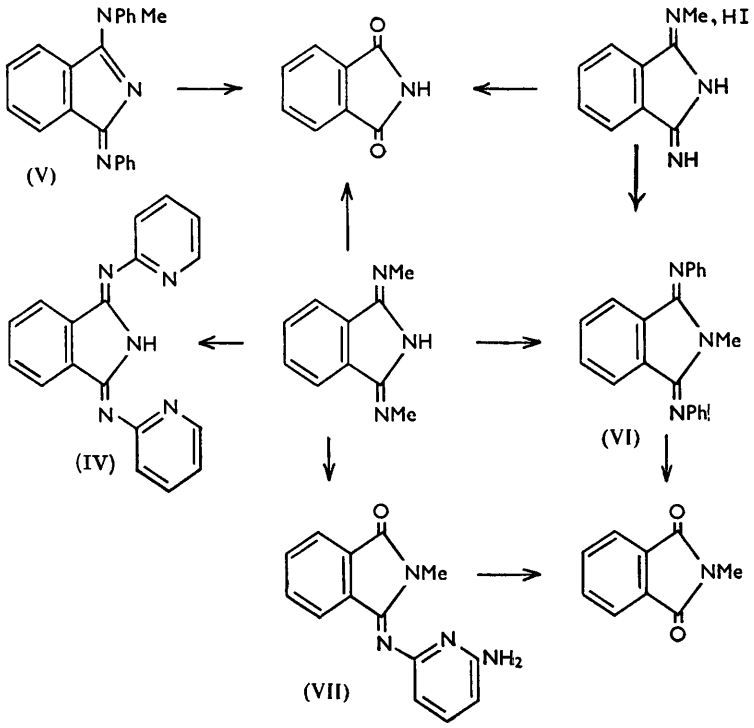
However, when 1 : 3-dimethyliminoisoindoline was heated with aniline (in contrast to aminopyridine) an unexpected reaction occurred. The product was, not the diphenyl-substituted imidine (I; R = R″ = Ph, R′ = H), but a methyl derivative which was isomeric with the known methyl derivative [2] (V). Hence the product evidently had the symmetrical 2-methyl-1 : 3-diphenylimino-structure (VI), and this was confirmed by its hydrolysis to *N*-methylphthalimide and 2 mols. of aniline. This condensation is thus accompanied by rearrangement and is of the type *b* (i). Similarly, the hydriodide of the monomethyl-imidine (I; R = Me, R′ = R″ = H) underwent rearrangement with aniline, to yield 2-methyl-1 : 3-diphenyliminoisoindoline (VI). A further example was the interaction of 1 : 3-dimethyliminoisoindoline and 2 : 6-diaminopyridine, which gave 3-(2-amino-6-pyridylimino)-2-methyl-1-oxoisoindoline (VII). A slight complication here was the incidental hydrolysis of one of the exocyclic nitrogen functions. The structure of the product was confirmed by its ready hydrolysis to *N*-methylphthalimide and 1 mol. of 2 : 6-diaminopyridine.

The yields of products from the various reactions were only 30—50%. We failed in each case to find other products, but obviously it remains uncertain that the reactions occur solely in the senses indicated. Indeed it appears, in general, that more than one reaction

[6] Elvidge and Linstead, *J.*, 1955, 3536.

course is open for any particular imidine–amine condensation. Further work on this topic is in hand.

Light Absorption and Fine Structure.—The ultraviolet light absorptions of the new imidine derivatives are given in the Table. Previous tentative generalisations [2,7] concerning the bond structures of imidines and their light absorptions are broadly confirmed. The conclusions are valid, of course, only if the various compounds compared have similar excited states. This seems probable within the limited field of phthalic imidine derivatives.



In the imino-imide series (II), the fully *N*-substituted (*i.e.*, fixed) *iso*indolines (II*A*) (see Table) have a maximum in the region of 3000 Å, irrespective of whether the substituents are alkyl, aryl, or heteroaryl. There is very little doubt therefore that the potentially tautomeric parent imino-imide [2] (II; R = R′ = H), its monomethyl derivative, their hydrochlorides, and the oxime [3] (II; R = OH, R′ = H) all exist in the bond form (II*A*). (It is presumably the exocyclic imino-group which is protonated in the salts.) The fixed alkyl-substituted *iso*indolenine (II*B*; RR′ = ·$[CH_2]_5$·), like the related morpholino-derivative,[2] has a maximum in the region of 3400 Å. The incompletely substituted *N*-aryl and *N*-heteroaryl derivatives (II; R′ = H) have maxima in the region of 3380—3830 Å.[1,2] The conclusion [2] that these exist in the form (II*B*) is fully justified: the only exception is the 3-pyridyl derivative (II; R = 3-C_5H_4N, R′ = H) which may be a tautomeric mixture of the forms *A* and *B* in solution. The variations in the position of the band of longest wavelength for the compounds (II*B*; R′ = H) indicate that *N*-substituents in the *iso*indolenine structure have appreciable auxochromic effects. This contrasts with the absence of substituent effects in the true *iso*indolines (II*A*).

In the di-imino*iso*indoline series (I) similar considerations appear to apply.

In this series we have prepared for the first time a compound with the fixed structure (I*A*), *viz.*, the derivative (VI). This shows a maximum at 3050 Å. In contrast, the isomer (V) and related *iso*indolenines [2] have maxima at 3680—3790 Å. Of particular

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

interest also is the alkyl-substituted *iso*indolenine (I*B*; R = R′ = R″ = Me) which was obtained in methanol solution from the hydriodide and 1 equivalent of sodium methoxide : the base shows an absorption maximum at 3480 Å.

Light absorptions in methanol and water.

Compound	$\lambda_{max.}$ (Å)	ε	Compound	$\lambda_{max.}$ (Å)	ε
(VI)	2270	26,400	(I; R = R″ = Et, R′ = H)	2650	11,100
	2580	19,900		3120	3,800
	2650				
	3050	9,600	(I; R = R″ = CH_2Ph, R′ = H)	2650	15,000
				3160	4,700
(V) [2]	2580	11,200			
	2680	12,400	(II*A*; R = R′ = Me)	2500	14,300
	2810			2980	3,500
	2900				
	3680	14,600	(II*A*; R = Ph, R′ = Me) [2]	2510	18,900
				2810	3,800
(I*B*; R = R′ = R″ = Me)	2790	12,200		2910	
	3480	3,900		3020	
,, ,HI	2270	31,500	(II*A*; R = 2-NH_2-6-pyridyl,		
	2800	12,900	R′ = Me)	2430	18,900
	3180 †	5,000		3030	7,000
	3540	3,800			
			(II; R = R′ = H),HCl [1]	* 2260	26,000
(I; R = R″ = Me, R′ = H)	2520	11,100		2980	1,000
	2660	14,000			
	3080	7,300	(II; R = Me, R′ = H),HCl	* 2480	16,100
				3060	3,900
,, ,, ,HCl	2725	17,000			
	3070	6,100	(II*B*; RR′ = ·$[CH_2]_5$·)	2620	10,000
	3350	3,900		3070	1,500
				3380	

* In H_2O; others in MeOH. † Inflexion.

The new results strongly suggest that the potentially tautomeric parent imidine (I; R = R′ = R″ = H), the dioxime [3] (I; R = R″ = OH, R′ = H), and the dimethyl derivative, which have maxima in the region of 3000 Å, exist entirely in the di-imino*iso*indoline form (I*A*). The other dialkyl derivatives (I) listed in the Table show maxima at slightly longer wavelengths, like the dibutyl compound [2] (I; R = R″ = Bu, R′ = H), so it appears that these tautomerise a little to the form (I*B*) in solution. In the *N*-aryl and *N*-heteroaryl derivatives [2] (I; R′ = H) the tautomeric form (I*B*) must predominate because these compounds all show absorption maxima above 3500 Å. It now seems that the individual variations in position of the longest-wavelength band are substituent effects, which appear in aminoimino*iso*indolenines (I*B*) but not in di-imino*iso*indolines (I*A*).

Experimental

Analyses were performed in the microanalytical laboratories (Mr. F. H. Oliver) and light absorption measurements were made in the spectrographic laboratory (Mrs. A. I. Boston) of this Department.

*Monomethyl Derivative of Di-imino*iso*indoline.*—The imidine [1] (I; R = R′ = R″ = H) (1 g.) was heated with methyl iodide (5 c.c.) at 80° for 18 hr. Recrystallisation of the substantially pure product (1·83 g., 100%) from dry methanol afforded yellow needles of 1-*imino*-3-*methylimino*iso*indoline hydriodide*, m. p. 250° (decomp.) (Found : C, 37·6; H, 4·0; N, 14·4. $C_9H_{10}N_3I$ requires C, 37·7; H, 3·5; N, 14·6%).

When this salt (414 mg.) was boiled with 2N-hydrochloric acid (5 c.c.) for 2 min. the yellow colour was discharged. The solution was then kept at 0° overnight. Phthalimide separated (132 mg., 0·63 mol.), having m. p. and mixed m. p. 232°.

1 : 3-*Dimethylimino*iso*indoline* (I; R = R″ = Me, R′ = H).—(a) *Preparation.* (i) A mixture of di-imino*iso*indoline (5 g.), dry ethanol (20 c.c.), and liquid methylamine (10 c.c.) was heated at 100° for 16 hr. The orange solution was evaporated to dryness under reduced pressure, the residue was dissolved in benzene, and the solution treated with charcoal. Concentration and

cooling of the solution afforded 1 : 3-*dimethyliminoisoindoline* (3·3 g., 56%), m. p. 168—169°, which crystallised from ethyl acetate as colourless needles, m. p. 172° (decomp.) [Found: C, 69·2; H, 6·7; active H ($LiAlH_4$ in Bu_2O), 0·57; N, 24·7. $C_{10}H_{11}N_3$ requires C, 69·3; H, 6·4; 1 active H, 0·58; N, 24·3%].

(ii) Phthalonitrile (5 g.), dry ethanol (20 c.c.), and liquid methylamine (10 c.c.) were heated at 100° for 24 hr. Treatment of the solution as in (i) yielded 1 : 3-dimethyliminoisoindoline (5·3 g., 78%) with m. p. 164—165° (decomp.), raised to 172° (decomp.) on recrystallisation from ethyl acetate.

The *picrate*, prepared in methanol and extractively crystallised from ethanol, formed yellow prisms, m. p. 264° (decomp.) (Found: C, 47·8; H, 3·7; N, 20·6. $C_{15}H_{12}O_7N_6$ requires C, 47·8; H, 3·5; N, 20·9%).

Treatment of the base in ethanol with ethereal hydrogen chloride, and crystallisation of the precipitate from water at 0° by addition of dioxan, afforded minute needles of the *hydrochloride*, m. p. 296° (decomp.) (Found: C, 57·1; H, 5·7; Cl, 16·8. $C_{10}H_{12}N_3Cl$ requires C, 57·3; H, 5·8; Cl, 16·9%).

(b) *Hydrolysis.* The base (282 mg.) with warm 2N-hydrochloric acid (3 c.c.) gave needles of a hydrochloride, but boiling the mixture for 5 min. afforded a clear solution. At 0° overnight, this deposited phthalimide (150 mg., 0·63 mol.), m. p. and mixed m. p. 234°. The intermediate 3-*methylimino*-1-*oxo*isoindoline *hydrochloride* (II; R = Me, R′ = H),HCl crystallised as needles, m. p. 319° (decomp.), from water on addition of ethanol (Found: C, 54·9; H, 4·7. $C_9H_9ON_2Cl$ requires C, 54·95; H, 4·6%).

Trimethyl Derivative of Di-iminoisoindoline.—1 : 3-Dimethyliminoisoindoline (1 g.) was heated with an excess of methyl iodide at 100° for 15 hr., and the solid product (1·64 g.), m. p. 260° (decomp.), was recrystallised five times from a 1 : 3 mixture of benzyl alcohol and ethanol: the 3-*dimethylamino*-1-*methyliminoisoindolenine hydriodide* (I*B*; R = R′ = R″ = Me),HI separated as yellow prisms (0·22 g.), m. p. 269—270° (decomp.) (Found: C, 41·7; H, 4·7; N, 12·9. $C_{11}H_{14}N_3I$ requires C, 41·9; H, 4·5; N, 13·3%). The salt (26·6 mg.) was boiled with 2N-hydrochloric acid (2 c.c.) for 2 min. and the solution was then kept overnight at room temperature. Phthalimide (4·8 mg., 0·39 mol.), m. p. and mixed m. p. 231°, separated.

Action of Methylamine on 3-*Imino*-1-*oxo*isoindoline (II; R = R′ = H).—This imino-imide [1] (4·5 g.), ethanol (15 c.c.), and liquid methylamine (10 c.c.) were heated together at 100° for 18 hr. The solution was treated with charcoal and was then concentrated, whereupon a white solid separated (3·8 g., 71%), having m. p. 136°. From methanol, 2-*methyl*-3-*methylimino*-1-*oxo*isoindoline (II*A*; R = R′ = Me) formed needles, m. p. 138·5° (Found: C, 69·2; H, 6·0; N, 16·4. $C_{10}H_{10}ON_2$ requires C, 68·9; H, 5·8; N, 16·1%).

Boiling the compound (72 mg.) with 2N-hydrochloric acid (2 c.c.) for 2 min. and cooling the solution at 0° overnight afforded *N*-methylphthalimide (59 mg., 0·89 mol.), m. p. and mixed m. p. 135°.

3-m-*Acetamidophenylimino*-1-*oxo*isoindoline (II; R = *m*-C_6H_4·NHAc, R′ = H).—*m*-Aminoacetanilide [8] (1 g.) and 3-imino-1-oxoisoindoline (1 g.) were boiled in ethanol (20 c.c.) for 17 hr. From ethanol, 3-m-*acetamidophenylimino*-1-*oxo*isoindoline (1·18 g., 61%) formed pale yellow needles, m. p. 245—246° (Found: C, 68·7; H, 4·8; N, 15·4. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·0%).

A suspension of the compound (500 mg.) in 2N-hydrochloric acid (20 c.c.) was stirred and heated on the steam-bath for 5 min. The mixture was then cooled and the mass of needles of phthalimide collected (228 mg., 0·86 mol.); they had m. p. 230—231° and mixed m. p. 231—232°. The filtrate was evaporated to dryness under reduced pressure, and the residue heated in pyridine (10 c.c.) with toluene-*p*-sulphonyl chloride (0·4 g.) for 30 min. on the steam-bath. The excess of pyridine was removed under reduced pressure, and the oily residue taken up in 2N-sodium hydroxide. The solution was filtered, cooled, and acidified, and the crystalline precipitate then triturated with aqueous sodium hydrogen carbonate. From aqueous ethanol, *NN*′-ditoluene-*p*-sulphonyl-*m*-phenylenediamine (223 mg., 0·31 mol.) crystallised as laths, m. p. and mixed m. p. 171—172°.

The *toluene*-p-*sulphonyl derivative* of *m*-aminoacetanilide formed parallelogrammic plates (from ethanol–water), m. p. 182° (Found: C, 59·05; H, 5·4; N, 9·4. $C_{15}H_{16}O_3N_2S$ requires C, 59·2; H, 5·3; N, 9·2%), and depressed the m. p. of the previous derivative to 149—160°.

1-*Oxo*-3-*piperidino*isoindolenine.—3-Imino-1-oxoisoindoline (2 g.), piperidine (3 c.c., redistilled), and ethanol (25 c.c.) were boiled together for 20 hr. The solution was treated with

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

charcoal and concentrated under reduced pressure, and the residue was triturated with light petroleum (b. p. 60—80°) and then dissolved in benzene (10 c.c.). When cooled, the solution deposited 1-*oxo*-3-*piperidino*iso*indolenine* (2·3 g., 78%), m. p. 137—140°, which on recrystallisation from ethyl acetate gave creamy-yellow prisms, m. p. 143° (Found: C, 73·1; H, 6·7; N, 13·7. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·6; N, 13·1%).

Action of Aqueous Ethylamine on 3-*Imino*-1-*oxo*iso*indoline.*—A solution of the imino-imide (1·45 g.) in ethanol (40 c.c.) and 30% aqueous ethylamine (1·5 c.c.) was heated on the steam-bath for 3 hr., and then evaporated. The residue was triturated with ether, and the solid extracted with benzene. Recrystallisation of the extract from benzene yielded *NN'*-diethylphthalamide, m. p. and mixed m. p. 161—162°.

1-*Imino*-3-*morpholino*iso*indolenine* (*IB*; RR' = ·$[CH_2]_2$·O·$[CH_2]_2$·, R'' = H).—Sodium (5 mg.) was treated with methanol (25 c.c.). Morpholine (1·74 g.) and phthalonitrile (2·56 g.) were added and the mixture was boiled for 3 hr. Traces of phthalocyanine (3·2 mg.) were removed and the filtrate was evaporated. The greenish crystalline residue (1·44 g.) was washed with acetone and dissolved in cold methanol, and, without delay, the solution was treated with charcoal and concentrated under reduced pressure, and the cream-coloured solid transferred to the filter with dioxan. Recrystallisation was effected by evaporating a methanol solution to very small bulk and then adding dioxan slowly: 1-*imino*-3-*morpholino*iso*indolenine* separated as pale cream-coloured prisms (0·8 g.), which became progressively darker blue above 100° without melting, and had an instantaneous melting-decomposition point at 174° (Found, on different preparations, dried at room temperature: C, 64·7, 64·7, 63·8; H, 5·6, 6·15, 6·3; N, 18·9, 19·2. $C_{12}H_{13}ON_3,\frac{1}{2}H_2O$ requires C, 64·3; H, 6·3; N, 18·7%). To the base (100 mg.) in methanol (1 c.c.), picric acid (107 mg.) in methanol (2 c.c.) was added. The precipitated *picrate* (188 mg.) had m. p. 240° (decomp.) (rapid heating) (Found: N, 19·3. $C_{18}H_{16}O_8N_6$ requires N, 18·9%).

The base (614 mg.) slowly dissolved (18 hr.) in water (2 c.c.) at room temperature. The solution smelled of morpholine, and during 2 days deposited 3-imino-1-oxo*iso*indoline (344 mg., 0·80 mol.), m. p. and mixed m. p. 205°.[2]

3-*Diethylamino*-1-*imino*iso*indolenine* (*IB*; R = R' = Et, R'' = H).—Phthalonitrile (2·56 g.) and diethylamine (1·46 g.) were added to methanol (25 c.c.) with which sodium (5 mg.) had reacted, and the mixture was boiled for 3 hr. Traces of phthalocyanine were filtered off, the solution was evaporated under reduced pressure, the crystalline residue was dissolved in ether, and the solution was treated with charcoal and then evaporated to small bulk. 3-Diethylamino-1-imino*iso*indolenine separated as pale yellowish crystals (0·5 g.), m. p. 59°. The *picrate*, prepared in ethanol, was crystallised extractively from ethanol to yield yellow needles, m. p. 212° (decomp.) (Found: C, 50·7; H, 4·5; N, 19·5. $C_{18}H_{18}O_7N_6$ requires C, 50·2; H, 4·2; N, 19·5%).

1 : 3-*Diethylimino*iso*indoline* (I; R = R'' = Et, R' = H).—A solution of phthalonitrile (5 g.) in ethanol (15 c.c.) containing dry ethylamine (10 c.c.) was heated at 100° for 36 hr. and then evaporated under reduced pressure. After 3 days at 0°, the residue crystallised: trituration with ether–light petroleum (b. p. 60—80°) afforded a cream-coloured solid (4·9 g., 63%), m. p. 154—155°. From ethyl acetate, the 1 : 3-*diethylimino*iso*indoline* formed colourless prisms, m. p. 158° (Found: C, 71·2; H, 7·4; N, 21·0. $C_{12}H_{15}N_3$ requires C, 71·6; H, 7·5; N, 20·9%).

Hydrolysis of the base (500 mg.) with boiling 2N-hydrochloric acid (5 c.c.) for 5 min. and cooling of the solution (4 hr. at 0°) afforded phthalimide (326 mg., 0·89 mol.) as needles, m. p. and mixed m. p. 230°.

1 : 3-*Dibenzylimino*iso*indoline* (I; R = R'' = CH_2Ph, R' = H).—Di-imino*iso*indoline (3 g.), ethanol (25 c.c.) and benzylamine (6 c.c.) were heated together under reflux for 24 hr. Ammonia was evolved. On evaporation of the solution under reduced pressure a semi-solid mass was obtained, which was drained on porous tile. Crystallisation of the solid (5·9 g.), m. p. 130—150°, from toluene provided 1 : 3-*dibenzylimino*iso*indoline* (5·1 g., 76%) as cream-coloured rods, m. p. 160° (Found: C, 81·3; H, 6·0; N, 13·1. $C_{22}H_{19}N_3$ requires C, 81·2; H, 5·9; N, 12·9%).

The base (247 mg.) was boiled in ethanol (2 c.c.) and 50% aqueous hydrochloric acid (2 c.c.) for 30 min. Water (5 c.c.) was added and the solution was concentrated under reduced pressure and cooled to 0°. Phthalimide separated (98 mg., 0·88 mol.), having m. p. and mixed m. p. 232°.

1 : 3-*Di*-m-*acetamidophenylimino*iso*indoline and* 3-m-*Acetamidophenylimino*-1-*imino*iso*indoline.*—Di-imino*iso*indoline (0·5 g.) and *m*-aminoacetanilide[3] (1 g.) were boiled in ethanol (40 c.c.) overnight, and the mixture was then cooled. The 1 : 3-*di*-m-*acetamidophenylimino*iso*indoline* (I; R = R'' = *m*-C_6H_4·NHAc, R' = H) (0·85 g.), m. p. 260°, was recrystallised from propylene carbonate to yield yellow prisms, m. p. 261° (decomp.), of a stable *hemihydrate* (Found,

in different preparations, dried at 140°/15 mm. for 2 hr. : C, 69·1, 68·2, 68·55; H, 5·3, 5·1, 5·2; N, 16·4, 16·55, 16·75. $C_{24}H_{21}O_2N_5,\frac{1}{2}H_2O$ requires C, 68·6; H, 5·3; N, 16·7%).

Evaporation of the filtrate from this product afforded 3-m-*acetamidophenylimino*-1-*imino*iso-*indoline* (I; R = *m*-C_6H_4·NHAc, R′ = R″ = H) (0·3 g.), m. p. 239°, which crystallised from ethanol as pale, slightly greenish, yellow prismatic needles, m. p. 240—241° (Found : C, 68·8; H, 5·2; N, 20·3. $C_{16}H_{14}ON_4$ requires C, 69·05; H, 5·1; N, 20·1%). The m. p. was depressed to 228° by 3-*m*-acetamidophenylimino-1-oxo*iso*indoline (above).

The 3-*m*-acetamidophenylimino-1-imino*iso*indoline (300 mg.) was stirred with concentrated hydrochloric acid (6 c.c.) and heated on the steam-bath for 10 sec.[2] The suspension was at once diluted with water, chilled, and poured into an excess of aqueous ammonia. The pale yellow precipitate (124 mg.) had m. p. 239—240° and mixed m. p. 241—244° with 3-*m*-acetamidophenylimino-1-oxo*iso*indoline (above).

3-*m*-Acetamidophenylimino-1-imino*iso*indoline (0·5 g.) and *m*-aminoacetanilide (0·27 g.) were boiled together in 2-methoxyethanol (10 c.c.) overnight. Evaporation of the solution and trituration of the residue with ethanol afforded 1 : 3-di-*m*-acetamidophenylimino*iso*indoline hemihydrate (0·2 g.), m. p. and mixed m. p. 261° (decomp.).

1 : 3-Di-*m*-acetamidophenylimino*iso*indoline (340 mg.) was boiled with 2N-hydrochloric acid (20 c.c.) for 15 min., and undissolved solid (74 mg.) removed. Cooling the filtrate to 0° afforded needles of phthalimide (103 mg., 0·86 mol.), m. p. and mixed m. p. 230—231°.

Displacement Reactions.—(i) 1-Imino-3-morpholino*iso*indolenine (I*B*; RR′ = ·$[CH_2]_2$·O·$[CH_2]_2$·, R″ = H) (455 mg.) in methanol (5 c.c.) was kept with aniline (197 mg.) for 24 hr. Yellow crystals separated : a second crop, obtained by concentration of the mother-liquors under reduced pressure, was washed with a little acetone. The product (217 mg., 46%) had m. p. 199—203° (decomp.) undepressed by 1-imino-3-phenylimino*iso*indoline (I; R = Ph, R′ = R″ = H), m. p. 203° (decomp.).[2]

(ii) 3-Diethylamino-1-imino*iso*indolenine (I*B*; R = R′ = Et, R″ = H) (1 g.) in ethanol (10 c.c.) with aniline (460 mg.) for 24 hr. similarly gave 1-imino-3-phenylimino*iso*indoline (I; R = Ph, R′ = R″ = H) (387 mg., 35%), m. p. and mixed m. p. 202° (decomp.).

(iii) 1-Imino-3-morpholino*iso*indolenine (433 mg.) and butylamine (5 c.c.) were heated under reflux until the evolution of ammonia slackened. The butylamine was evaporated off, the residue taken up in ether, and the solution treated with charcoal. Concentration of the filtrate afforded needles of 1 : 3-dibutylimino*iso*indoline (I; R = R″ = Bu, R′ = H) (133 mg.), m. p. and mixed m. p. 132°.[2]

(iv) Similarly, 3-diethylamino-1-imino*iso*indolenine (1 g.) and boiling butylamine afforded 1 : 3-dibutylimino*iso*indoline (720 mg., 56%), m. p. and mixed m. p. 131—132°.

(v) 3-Morpholino-1-oxo*iso*indolenine [2] (II*B*; RR′ = ·$[CH_2]_2$·O·$[CH_2]_2$·) (500 mg.) in ethanol (10 c.c.) was heated under reflux with aniline (0·5 g.) for 17 hr. No ammonia was evolved. Evaporation of the solution to small bulk, and cooling, afforded 1-oxo-3-phenylimino*iso*indoline (II; R = Ph, R′ = H) (396 mg., 77%), m. p. and mixed m. p. 168—171°.[1]

(vi) 1-Imino-3-phenylimino*iso*indoline (I; R = Ph, R′ = R″ = H) (2 g.), butylamine (5 c.c.), and ethanol (10 c.c.) were boiled together for 18 hr. Ammonia was evolved. The solution was evaporated, the residue was taken up in ether, and light petroleum (b. p. 40—60°) added. Crystallisation of the precipitate from *cyclo*hexane (charcoal) gave yellow needles (1·14 g., 49%), m. p. 128—129°, of 1 : 3-dibutylimino*iso*indoline (I; R = R″ = Bu, R′ = H), which had m. p. and mixed m. p. 130° after a recrystallisation (Found : C, 75·1; H, 9·2; N, 16·9. Calc. for $C_{16}H_{13}N_3$: C, 74·7; H, 9·0; N, 16·3%).

(vii) 1 : 3-Dimethylimino*iso*indoline (2 g.) and 2-aminopyridine (4 g.) were boiled together in ethyl carbitol (diethylene glycol ethyl ether) (7·5 c.c.) for 11 hr. Methylamine was evolved. Evaporation under reduced pressure yielded a brown gum which was dissolved in benzene. The solution was treated with charcoal and then chromatographed on a column (12 × 3·5 cm.) of alumina (Brockmann grade II). The first, fast-moving yellow band was eluted with benzene (500 c.c.). Evaporation of the eluate afforded a yellow solid. Other brown bands on the column provided intractable oils. Rechromatography of the solid in benzene on a similar column, and elution with benzene (1250 c.c.) and 10% chloroform–benzene (750 c.c.) provided 1 : 3-di-2′-pyridylimino*iso*indoline [1] (IV) (162 + 330 mg.), m. p. and mixed m. p. 179—180° after recrystallisation from ethanol. Further elution of the column with 20% acetone–benzene (300 c.c.) yielded 2-aminopyridine (60 mg.), m. p. and mixed m. p. 54° after a recrystallisation from light petroleum (b. p. 40—60°).

Condensations with Rearrangement.—(i) 1 : 3-Dimethylimino*iso*indoline (596 mg.), aniline (2 c.c.), and ethyl carbitol (5 c.c.) were heated together under reflux. Methylamine was evolved.

After 5 hr., the solution was evaporated under reduced pressure, and the residual gum was triturated with light petroleum (b. p. 60—80°) and then dissolved in ethanol. The solution was treated with charcoal and evaporated, and the residue was taken up in benzene (15 c.c.) and chromatographed on a column (12 × 3·5 cm.) of alumina (Brockmann grade II). The eluate which contained the material of the slower-moving of the two yellow bands was rechromatographed similarly. Evaporation of the final eluate yielded 2-*methyl*-1 : 3-*diphenyliminoisoindoline* (VI) (201 mg.) which crystallised from ethanol as lemon-yellow leaflets (66 mg.), m. p. 190—191° (Found : C, 81·1; H, 5·6; N, 13·8. $C_{21}H_{17}N_3$ requires C, 81·0; H, 5·5; N, 13·5%). No other solid product was isolated. Repetition of the condensation in boiling ethanol for 24 hr. gave 2-methyl-1 : 3-diphenyliminoisoindoline in much poorer yield.

1-Imino-3-methyliminoisoindoline hydriodide (1 g.) was boiled in ethanol (25 c.c.) with aniline (2·5 c.c.). Ammonia was evolved. After 12 hr., the solution was concentrated under reduced pressure to 15 c.c., and cooled. 2-Methyl-1 : 3-diphenyliminoisoindoline (VI) (0·32 g.) separated; its m. p. and mixed m. p. (190—191°) were unchanged on recrystallisation from aqueous ethanol (Found : C, 80·9; H, 5·5; N, 13·5%). Chromatography of the material of the mother-liquors, in benzene on alumina, as previously, provided a less pure second crop (0·25 g.), m. p. 175—180°.

2-Methyl-1 : 3-diphenyliminoisoindoline (VI) (53·4 mg.) in ethanol (1 c.c.) was warmed on the steam-bath with 2N-hydrochloric acid (2 c.c.) for 10 min. Cooling the solution caused the separation of colourless needles of *N*-methylphthalimide (21·2 mg., 0·77 mol.), m. p. and mixed m. p. 131°. Diazotisation of the filtrate and addition of aqueous alkaline β-naphthol yielded phenylazo-β-naphthol (70·5 mg., 1·77 mol.) as dark red needles, m. p. and mixed m. p. 129°.

(ii) 1 : 3-Dimethyliminoisoindoline (1·7 g.) and 2 : 6-diaminopyridine (3·4 g.) were boiled together in ethyl carbitol (10 c.c.) for 17 hr. Removal of the solvent under reduced pressure left a black tar which was taken up in acetone (100 c.c.). The solution was filtered, treated with charcoal, and evaporated. The residue was dissolved in 10% acetone-in-benzene (50 c.c.), and the solution was filtered and then chromatographed on a column (12 × 3·5 cm.) of alumina (Brockmann grade II). Development of the chromatogram with the same solvent afforded a brown, an orange and a (fastest) yellow band. Elution of the material of the yellow zone with the same solvent (1500 c.c.), evaporation of the eluate, and draining of the residue on porous tile gave a crude yellow powder (1·04 g.). Continuous extraction of this with light petroleum (b. p. 80—100°) for 36 hr. removed a little 2 : 6-diaminopyridine. Crystallisation of the residue from benzene (charcoal) and then from toluene provided 3-(2-*amino*-6-*pyridylimino*)-2-*methyl*-1-*oxo*-iso*indoline* (VII) as orange-yellow needles, m. p. 198° (decomp.) [Found : C, 66·2; H, 4·8; N, 22·0%; *M* (Rast), 253. $C_{14}H_{12}ON_4$ requires C, 66·7; H, 4·8; N, 22·2%; *M*, 252]. From the middle zone of the column, a trace of red gum was eluted. From the top brown band, 10% ethanol-in-benzene (900 c.c.) eluted a reddish tar (1·3 g.) from which boiling ligroin (b. p. 100—120°) extracted 2 : 6-diaminopyridine (0·4 g.), m. p. and mixed m. p. 120°.

3-(2-Amino-6-pyridylimino)-2-methyl-1-oxoisoindoline (44 mg.) was warmed on the steam-bath with 2N-hydrochloric acid (1 c.c.) for 20 min., by which time the colour was discharged. After 2 hr. at 0°, needles of *N*-methylphthalimide (21·6 mg., 0·77 mol.) had separated (m. p. 130° and mixed m. p. 132°). Treatment of the filtrate with a saturated solution of picric acid in ethanol (1 c.c.) caused precipitation of 2 : 6-diaminopyridine picrate (36 mg., 0·61 mol.), m. p. and mixed m. p. 236°.

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