Heterocyclic Imines and Amines. Part IV. Imidines from* 3 : 4 : 5 : 6-*Tetrahydrophthalic Acid and* cis-*Hexahydrophthalic Acid. An Unusual Dehydrogenation.*

By G. E. Ficken and R. P. Linstead.

[Reprint Order No. 6282.]

The preparation of 3 : 4 : 5 : 6-tetrahydrophthalimidine and of *cis*-hexahydrophthalimidine from the corresponding nitriles is described. The structures are established by hydrolysis. The imidines react with two mols. of primary bases with evolution of ammonia. The products have the expected structures except that the same diphenylimino-compound is obtained from both imidines, a novel type of dehydrogenation occurring with the hexahydro-compound. The properties, including light-absorption data, of the imidines and their derivatives are described and a preliminary account is given of their easy conversion into tetrazaporphin pigments.

It has been shown in earlier papers of this series (Elvidge and Linstead, *J.*, 1952, 5000; 1954, 442) that phthalonitrile and succinonitrile can, under suitable conditions, add the elements of ammonia to yield heterocyclic compounds, the imidines. This new class of compound has an interesting and specific chemistry of its own. In particular, the imidines are valuable precursors of tetrazaporphin pigments. We now report the preparation of the first imidine of the maleic acid series, 3 : 4 : 5 : 6-tetrahydrophthalimidine; also the related hexahydrophthalimidine. There is a considerable difference between the saturated and the unsaturated compound and we shall deal with the latter first, as the less complicated.

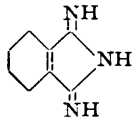
3 : 4 : 5 : 6-Tetrahydrophthalonitrile (Linstead and his co-workers, *J.*, 1952, 4846; 1954, 3730) readily adds ammonia in a boiling methanol solution containing a trace of sodium methoxide.† The product is a strong base, $C_8H_{11}N_3$, comparatively stable, and easily crystallised from ethanol or dimethylformamide. It is sparingly soluble in cold water and not apparently hydrolysed. It yields a monopicrate and a dihydrochloride. It does not melt but decomposes fairly sharply at 177—180° with the formation of (*inter al.*) tetra*cyclo*hexenotetrazaporphin. It is clearly the imidine (I) of tetrahydrophthalic acid from its method of preparation and because it is readily hydrolysed by boiling water first to the imino-imide (II; R = H) and more slowly to tetrahydrophthalimide (III). This formulation is also supported by the reactions with primary bases reported below. Two tautomeric structures can be written for the imidine, the di-imine (I*a*) and the imino-amine (I*b*). The diaminopyrrole type, a third possibility for the imidines of saturated acids, cannot apply here. We do not regard the available evidence on the fine structure as being conclusive and it is receiving further study. For the present the di-imine structure (I*a*) sufficiently accounts for the properties of the compound.

The imino-imide (II; R = H; Δ^8-hexahydro-1-imino-3-oxo*iso*indole) is also obtained by thermal isomerisation of 2-cyano-3 : 4 : 5 : 6-tetrahydrobenzamide (Ficken and Linstead, *J.*, 1952, 4846). It yields a monopicrate and a monohydrochloride. Like the related

* Part III, *J.*, 1954, 442.

† This modification of earlier methods is due to Imperial Chemical Industries Limited, Dyestuffs Division.

imino-imides investigated by Elvidge and Linstead (*loc. cit.*) it reacts with primary bases with elimination of ammonia. A phenylimino-compound (II; R = Ph) and an oximino-compound (II; R = OH) were formed in this way.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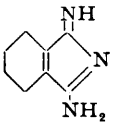
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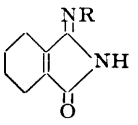
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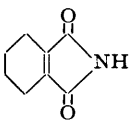
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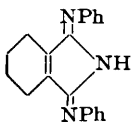
3 : 4 : 5 : 6-Tetrahydrophthalimidine also reacted readily with an excess of aniline or hydroxylamine, the products being the double condensation products (IV and V).

Hexahydrophthalimidine was less readily prepared than the tetrahydro-analogue. The method described above gave little or no product when applied to *cis*-hexahydrophthalonitrile and, although reaction with methanolic ammonia at higher temperatures gave some imidine, the yield was variable and never over 10%. The main trouble is the great reactivity of the hexahydroimidine which, even at 90°, tends to eliminate ammonia with the formation of aza-linked macrocyclic pigment and polymeric material. Below this temperature, reaction of the nitrile with ammonia is slow. Another difficulty is the great ease of hydrolysis of the imidine; on several occasions only the corresponding imino-imide was isolated. However, an alternative process, described by Elvidge and Linstead (*loc. cit.*, 1953) for the preparation of succinimidine, was successful, and when *cis*-hexahydrophthalonitrile was treated with a solution of sodamide in formamide the required imidine (octahydro-1 : 3-di-imino*iso*indole) (VI, or an isomer) crystallised from the reaction mixture in up to 70% yield.

Hexahydrophthalimidine is unstable and highly reactive. Prepared as described above, it forms colourless needles but it soon acquires a blue tinge, particularly when dried under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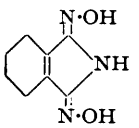
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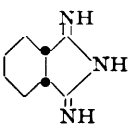
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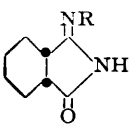
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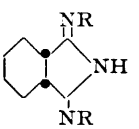

(VIII)

reduced pressure. The crystalline reaction product analysed for a hemihydrate, the water being lost at 10^{-5} mm. The base has no definite melting point. It forms a beautifully crystalline anhydrous monopicrate and a dihydrochloride. The imidine is hydrolysed when exposed to moist air and must be kept in a desiccator or a sealed vessel (unlike the tetrahydrophthalimidine, which seems to be indefinitely stable on the bench). Hexahydrophthalimidine dissolves readily in cold water with rapid hydrolysis to octahydro-1-imino-3-oxo*iso*indole (VII; R = H). The product is identical with the imino-imide described by Ficken, France, and Linstead, *J.*, 1954, 3730 and is hydrolysed by boiling water to *cis*-hexahydro-phthalimide. The imidine therefore has the *cis*-configuration.

trans-Hexahydrophthalonitrile reacts rather slowly with sodamide in formamide to yield an imidine indistinguishable from that described above. It gave the same picrate and was hydrolysed to the *cis*-imino-imide.

cis-Hexahydrophthalimidine reacts readily with hydroxylamine to give the dioximino-compound (VIII; R = OH). Reaction with aniline in boiling ethanol also leads to evolution of ammonia. The product, however, *is not the expected diphenylimine* (VIII; R = Ph) *but its dehydrogenation product*, that is the diphenylimine (IV) already obtained from 3 : 4 : 5 : 6-tetrahydrophthalimidine. This remarkable dehydrogenation has been repeated several times and we have no doubt as to its authenticity. A correspondingly easy passage from hexahydro- to tetrahydro-phthalic derivatives has not been observed with the parent imidine or the dioxime. The change, embodying, as it does, the introduction of a double bond into a substituted succinic acid system, is of considerable general interest. It is being investigated further. The fate of the extruded hydrogen is unknown; aerial oxygen is a possible acceptor.

The ultraviolet absorption data for these new compounds are summarised in the Table. It will be seen that the light absorption of the hexahydro-compounds closely resembles that of the corresponding succinic derivatives (Elvidge and Linstead, *loc. cit.*, 1953). The question of fine structure is reserved for a later communication.

As has already been said, both these imidines, particularly *cis*-hexahydrophthalimidine, are intermediates in the formation of tetrazaporphins. A little tetra*cyclo*hexenotetrazaporphin (Ficken and Linstead, *loc. cit.*, 1952) is formed when the tetrahydrophthalimidine is prepared from the corresponding nitrile. When an alcoholic solution of the hexahydro-imidine is boiled, a magenta colour develops. This is stable when the solution is cooled in an inert atmosphere but becomes pale green in air. Prolonged boiling of a solution, especially in a higher-boiling alcohol, gives first an irreversible purple colour and subsequently deposition of solid pigment. The product is a mixture of tetra*cyclo*hexenotetrazaporphin (main bands at 628 and 560 mμ) and a blue hydrogenated pigment (bands

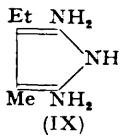
	3 : 4 : 5 : 6-*Tetrahydrophthalic series.*			cis-*Hexahydrophthalic series.*		
Compound	Formula	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$	Formula	$\lambda_{max.}$ (mμ)	$10^{-3}\varepsilon$
Imino-imide	II; R = H	240	10·5	VII; R = H	227	16·4
Oxime from imino-imide	II; R = OH	270 *	13·1	VII; R = OH	220	9·6
		281	13·8		227	
Phenylimine from imino-imide	II; R = Ph	251	19·2	VII; R = Ph	227	11·2
		256	16·3		257	8·9
		282	4·5		268	9·6
		294	4·1		279	8·9
		304				
		324	3·2			
		343				
Imidine	I	251	15·9	VI	242	17·4
		258	14·5			
Dioxime from imidine	V	298	17·9	VIII; R = OH	228	16·5
Diphenylimine from imidine	IV	228	16·0			
		251	12·9			
		266	14·5			
		270	9·0			
		280	7·8			
		333	4·2			

* Inflexion.

at 691·5 and 532 mμ). At higher temperatures, particularly in the presence of an oxidising agent, pigment formation is faster and more complete. In a boiling mixture of dichlorobenzene and nitrobenzene, hexahydrophthalimidine gave a 53% yield of tetra*cyclo*hexenotetrazaporphin. The same pigment is formed when the imidine (which has no sharp point of melting or decomposition) is heated to 125°. These ready formations of the tetrazaporphin ring without the intervention of metallic reagents are noteworthy.

These and similar reactions are being studied further.

Endermann and Hans Fischer (*Annalen*, 1939, **538**, 183) prepared 2 : 5-diamino-3-ethyl-4-methylpyrrole (IX) from the corresponding diazide. The diamine, when heated, liberated ammonia and gave a pigment to which the tetraza*ætio*porphyrin structure was assigned. (The yield is not stated; the same pigment was made in 0·2% yield from the corresponding di*iso*cyanate.) This formulation is certainly correct, for we have shown that the light absorption of the Endermann–Fischer pigment is virtually identical with that of our compound for which the tetra*cyclo*hexenotetrazaporphin structure has been conclusively proved (*loc. cit.*, 1952). It is possible that the Endermann–Fischer precursor has the di-imine or the amino-imine rather than the diaminopyrrole structure (IX).



(IX)

Experimental

3 : 4 : 5 : 6-*Tetrahydrophthalimidine* (Δ⁸-*Hexahydro*-1 : 3-*di*-*imino*iso*indole*).—3 : 4 : 5 : 6-Tetrahydrophthalonitrile (4·70 g.) was heated in a stream of ammonia gas in boiling methanol (50 ml.) containing sodium (8 mg.). After 12 hr. the hot solution was filtered to remove tetra*cyclo*hexenotetrazaporphin (130 mg., 3%; identified spectroscopically), and the filtrate was

boiled with charcoal and refiltered. The filtrate was evaporated to dryness under reduced pressure and the residue was washed with cold ethyl acetate and then with ether. This left a pale brown solid (3·64 g., 69%). After two crystallisations from ethanol or preferably dimethylformamide 3 : 4 : 5 : 6-*tetrahydrophthalimidine* (I) was obtained as colourless plates (Found : C, 64·55; H, 7·7; N, 28·2. $C_8H_{11}N_3$ requires C, 64·4; H, 7·4; N, 28·2%). When the solid was heated, slight darkening began at about 165°, and rapid decomposition at 177—180°. The *picrate*, prepared in ethanol, had m. p. 202—204° (decomp.) (Found : C, 44·8; H, 4·4; N, 21·9. $C_{14}H_{14}O_7N_6$ requires C, 44·45; H, 3·7; N, 22·2%). A filtered solution of the base in ethanol was poured into ethereal hydrogen chloride, and the precipitate of *dihydrochloride monohydrate* was filtered off and washed with ether (Found : C, 39·7; H, 6·5; N, 17·3; Cl, 30·0. $C_8H_{11}N_3,2HCl,H_2O$ requires C, 40·0; H, 6·3; N, 17·5; Cl, 29·5%).

The free base (930 mg.) was set aside in cold water (10 ml.) for 18 hr. No apparent change occurred and the recovered solid was unchanged imidine, decomp. 175°. It was added to the filtrate which was then brought to the boil and cooled immediately. The solution was evaporated to dryness, and the residue was washed with boiling ether, to give Δ^8-hexahydro-1-imino-3-oxo*iso*indole (II; R = H) (440 mg.), m. p. 188—194° (decomp.), the mixed m. p. with material prepared as described below undepressed; the picrate had m. p. and mixed m. p. 188—189° (decomp.). The di-imine (164 mg.) was boiled with water (3 ml.) for 8 hr., and the solution was evaporated to dryness to give tetrahydrophthalimide, m. p. and mixed m. p. 168—170°.

2-Cyano-3 : 4 : 5 : 6-tetrahydrobenzamide (5·85 g.) (Ficken and Linstead, *loc. cit.*,) was heated at 165—170° for 30 min., by which time the dark melt had almost completely resolidified. The product was boiled with ethanol (50 ml.), cooled, and filtered, to yield a pale brown solid, m. p. 193—198° (decomp.) (1·31 g.). After crystallisation from 2-ethoxyethanol (" Cellosolve ") Δ^8-*hexahydro*-1-*imino*-3-*oxo*isoindole was obtained colourless and had m. p. 200—202° (decomp.) (Found : C, 63·75; H, 6·8; N, 18·6. $C_8H_{10}ON_2$ requires C, 64·0; H, 6·7; N, 18·7%). The filtrate from the above preparation was evaporated to small volume and diluted with ethyl acetate, a second crop (1·05 g.) of slightly less pure material, m. p. 191—197°, being obtained. The *picrate*, crystallised from Cellosolve–ethanol, had m. p. 190—191° (decomp.) (Found : C, 44·5; H, 3·85; N, 18·5. $C_{14}H_{13}O_8N_5$ requires C, 44·3; H, 3·45; N, 18·5%). A solution of the keto-imine in ethanolic hydrogen chloride was evaporated to dryness under reduced pressure; the *hydrochloride*, crystallised from ethanol–ethyl acetate, had m. p. 250° (decomp.) (Found : N, 15·0; Cl, 19·8. $C_8H_{11}ON_2Cl$ requires N, 15·0 Cl, 19·0%).

The free keto-imine (II; R = H) (520 mg.) and hydroxylamine hydrochloride (350 mg.) were refluxed in "Cellosolve" (3 ml.) for 6 hr. The solvent was removed under reduced pressure and the residue was washed with water, to yield Δ^8-*hexahydro*-1-*hydroxyimino*-3-*oxo*isoindole (II; R = OH) (320 mg.), m. p. 245—246° (decomp.) after crystallisation from dilute ethanol (Found : C, 57·8; H, 6·3; N, 16·7. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·1; N, 16·9%). The keto-imine (430 mg.), aniline (290 mg.), and " Cellosolve " (3 ml.) were refluxed for 6 hr. and the solvent was removed under reduced pressure. The residue was sublimed at 160°/0·3 mm. and the sublimate (350 mg.) was crystallised from aqueous ethanol. Δ^8-*Hexahydro*-1-*oxo*-3-*phenyl*-*imino*iso*indole* (II; R = Ph) crystallised in pale yellow needles, m. p 128—129°, from light petroleum (b. p. 60—80°) (Found : C, 74·2; H, 6·4; N, 12·3. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2; N, 12·4%).

A solution of the imidine (I) (440 mg.) and hydroxylamine hydrochloride (490 mg.) in ethanol (5 ml.) was refluxed for 8 hr. On cooling, Δ^8-*hexahydro*-1 : 3-*dihydroxyimino*isoindole (V) separated, and after crystallisation from dilute acetic acid had m. p. 252—253° (decomp.) (Found : C, 53·0; H, 6·4; N, 23·2. $C_8H_{11}O_2N_3$ requires C, 53·0; H, 6·1; N, 23·2%). A solution of the imidine (I) (290 mg.) and aniline (400 mg.) in ethanol (5 ml.) was refluxed for 40 hr. The solvent was removed and the residue was chromatographed on alumina in benzene; the yellow band was eluted and yielded Δ^8-*hexahydro*-1 : 3-*diphenyliminoisoindole* (IV) (360 mg.) as pale yellow needles, m. p. 146·5—147·5° after crystallisation from aqueous ethanol (Found : C, 79·45; H, 6·5; N, 13·9. $C_{20}H_{19}N_3$ requires C, 79·7; H, 6·35; N, 13·9%).

cis-*Hexahydrophthalimidine* (VI) (cis-*Octahydro*-1 : 3-*di*-*imino*isoindole).—*cis*-Hexahydrophthalonitrile (6·7 g.) was dissolved in a solution of sodamide (3·9 g.) in dry formamide (35 ml.), and the solution left at room temperature for 2 days and then at 0° for 6 days. During this time the *imidine* (VI) crystallised as a hemihydrate in colourless needles, which were filtered off, washed with a little formamide, followed by ethyl acetate, and dried in a vacuum-desiccator (Found : C, 60·15; H, 8·5; N, 26·3. $C_8H_{13}N_3,\frac{1}{2}H_2O$ requires C, 60·0; H, 8·8; N, 26·2%). The yield was 5·2 g. (68%). The imidine was kept in a vacuum-desiccator over concentrated sulphuric acid, and slowly became blue. It did not melt, but began to become blue above 100°,

rapidly above 125°; the product in pyridine showed absorption bands due to tetra*cyclo*hexenotetrazaporphin (6270 and 5600 Å) (Ficken and Linstead, *loc. cit.*) and a hydrogenation product * (6915 and 5320 Å). The *imidine picrate*, prepared in absolute ethanol and crystallised from the same solvent in long yellow needles, had m. p. 209—210° (decomp.) (Found: C, 44·4; H, 4·5; N, 22·0. $C_{14}H_{16}O_7N_6$ requires C, 44·2; H, 4·2; N, 22·1%). The m. p. was depressed on admixture with 3 : 4 : 5 : 6-tetrahydrophthalimidine picrate to 194—196° (decomp.). The *dihydrochloride monohydrate* had m. p. 201—204° (decomp.) (Found: C, 39·1; H, 7·1; N, 17·4; Cl, 29·5. $C_8H_{13}N_3,2HCl,H_2O$ requires C, 39·7; H, 7·1; N, 17·4; Cl, 29·3%).

The imidine (210 mg.) readily dissolved in cold water. The solution soon smelt strongly of ammonia, and a white solid crystallised. This was filtered off after 4 hr. (76 mg.) and identified as *cis*-octahydro-1-imino-3-oxo*iso*indole (VII; R = H) by its m. p. and mixed m. p. 225—227° (decomp.). Evaporation of the filtrate at room temperature gave a further crop (92 mg.), m. p. 218—222° (decomp.). Both crops gave the same picrate, m. p. and mixed m. p. with the keto-imine picrate 204—206° (decomp.). The di-imine (320 mg.) was boiled with water for 6 hr., to yield *cis*-hexahydrophthalimide (290 mg.), m. p. 123—134°, raised to 135—137° by crystallisation from water.

Reaction of trans-*Hexahydrophthalonitrile with Sodamide.*—*trans*-Hexahydrophthalonitrile (2·41 g.) was added to sodamide (2·0 g.) in formamide (15 ml.), and the solution left for 4 days at room temperature and then at 0° for 8 days; the imidine (0·70 g.) was isolated as before and dried at room temperature at 10^{-5} mm. for 24 hr. This gave the anhydrous *imidine* (Found: C, 63·1; H, 8·6; N, 27·4. $C_8H_{13}N_3$ requires C, 63·5; H, 8·7; N, 27·8%). The picrate had m. p. 206—207° (decomp.) and mixed m. p. 208—209° with that of the di-imine from the *cis*-nitrile. The free base with cold water gave *cis*-octahydro-1-imino-3-oxo*iso*indole, m. p. 190—208° (decomp.) [picrate, m. p. 201—204° (decomp.) and mixed m. p. 202—205° (decomp.)].

*Tetra*cyclo*hexenotetrazaporphin from* cis-*Hexahydrophthalimidine.*—The imidine (VI) (615 mg.), *o*-dichlorobenzene (4·0 ml.), and nitrobenzene (1·0 ml.) were refluxed together. The solution became red immediately and then rapidly purple. Ammonia was copiously evolved and a blue solid was soon deposited. After 1 hr. the mixture was diluted with ethanol, and the solid was filtered off and washed with boiling ethanol. The yield of tetra*cyclo*hexenotetrazaporphin was 283 mg. (53%) (Found: N, 21·1. Calc. for $C_{32}H_{34}N_8$: N, 21·1%).

Reaction of the Imidine (VI) *with Bases.*—The imidine (530 mg.) and hydroxylamine hydrochloride (550 mg.) were refluxed in ethanol (5 ml.) for 22 hr. The solvent was removed and the residue was washed with a little cold water, to yield cis-1 : 3-*octahydrodihydroxyimino*iso*indole* (VIII; R = OH) (250 mg.), m. p. 168—171° (decomp.) after crystallisation from ethyl acetate (Found: C, 52·2; H, 7·35; N, 22·8. $C_8H_{13}O_2N_3$ requires C, 52·4; H, 7·15; N, 22·9%).

The imidine (VI) (385 mg.) and aniline (505 mg.) in ethanol (5 ml.) were refluxed for 66 hr. The solution was filtered to remove a little pigment, and the filtrate was evaporated to dryness. The product was chromatographed in benzene on alumina, and the yellow band was eluted, to yield Δ^8-hexahydro-1 : 3-diphenyliminoisoindole (IV) (110 mg.), m. p. 134—138°; the m. p. was raised to 144—145° by crystallisation from aqueous ethanol, and was undepressed on admixture with authentic material.

Condensations with cis-*Octahydro*-1-*imino*-3-*oxo*iso*indole* (VII; R = H).—The keto-imine (370 mg.), hydroxylamine hydrochloride (220 mg.), and "Cellosolve" (5 ml.), refluxed for 16 hr., gave cis-*octahydro*-1-*hydroxyimino*-3-*oxo*iso*indole* (VII; R = OH), m. p. 216—218° (decomp.) after crystallisation from aqueous ethanol (Found: C, 57·4; H, 7·3; N, 16·6. $C_8H_{12}O_2N_2$ requires C, 57·1; H, 7·2; N, 16·7%). The same keto-imine (650 mg.), aniline (450 mg.), and "Cellosolve" (8 ml.) were refluxed for 36 hr., the solution was evaporated to dryness, and the residue was washed with ether. The yield of cis-*octahydro*-1-*oxo*-3-*phenylimino*iso*indole* (VII; R = Ph) was 320 mg. and the m. p. after crystallisation from aqueous ethanol was 190—193° (Found: C, 73·8; H, 7·3; N, 12·65. $C_{14}H_{16}ON_2$ requires C, 73·65; H, 7·1; N, 12·3%).

We thank Imperial Chemical Industries Limited, Dyestuffs Division, for gifts of chemicals. Analyses were carried out in the microanalytical laboratory (Mr. F. H. Oliver), and spectrographic determinations in the spectrographic laboratory (Mrs. A. I. Boston), of the Department. We are grateful to Dr. J. A. Elvidge for helpful discussion.

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* The hydrogenation of tetrazaporphins will be described in a later communication.