187. *Phthalocyanines. Part IX. Derivatives of Thiophen, Thionaphthen, Pyridine, and Pyrazine, and a Note on the Nomenclature.*

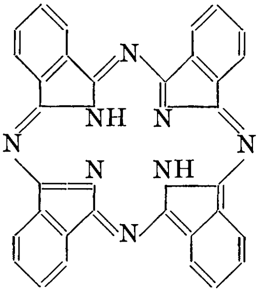
By R. P. Linstead, E. G. Noble, and J. M. Wright.

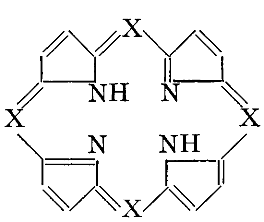
This and the three following papers are concerned with investigations of the chemistry of phthalocyanines in two main directions: (1) the possibility of obtaining similar compounds from heterocyclic instead of aromatic intermediates has been examined (Parts IX and X); (2) efforts have been made to bridge the gap between phthalocyanines and porphyrins.

The resemblance between these two groups has already been discussed (J., 1934, 1033; *Ann. Reports*, 1935, **32**, 359). The differences between the basic structures are two: phthalocyanine (*P*) contains four additional fused benzene rings and four linking nitrogen atoms in place of the four methene groups of porphin (*Q*, X = CH). To connect the two series more closely we have examined the possibility of preparing (*a*) compounds resembling phthalocyanine with nitrogen links but possessing no fused benzene rings (Part X), and (*b*) benzporphyrins, *i.e.*, analogous compounds with methene links and fused benzene rings (Part XI).

This extension of the field has created the need for a more precise nomenclature. The name phthalocyanine is now well established for compounds of the general type indicated by formula (*P*). It is proposed to use the term *porphyrazine* for the central ring system of the phthalocyanine molecule, that is, for the structure represented by formula (*Q*, X = N). Individual compounds are named by attaching an appropriate prefix. Thus the systematic name for phthalocyanine itself on this basis is tetrabenzporphyrazine and the corresponding compound with four pyridine rings in place of four benzenes becomes tetrapyridinoporphyrazine. To avoid undue complication it is not proposed to use the systematic names for simple phthalocyanines, but they have been employed in naming the heterocyclic compounds and derivatives of maleic acid in the papers which follow.

(*P.*)

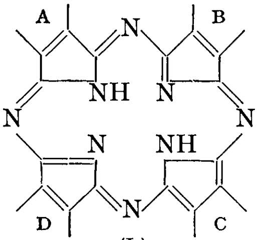




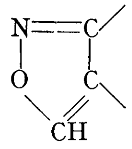
(*Q.*)

On theoretical grounds it is to be anticipated that there will be considerable differences in the ease with which phthalocyanine-like compounds are formed from *o*-dinitriles derived from various heterocyclic compounds. The most important factors which may be expected to influence the reaction are reviewed below.

(1) The common porphyrazine framework is represented in (I), where A, B, C and D indicate the position of four heterocyclic rings. This formula is not, however, fully adequate, as the molecule is in all probability a resonance hybrid between a number of similar structures, of which one is represented by formula (I), which is equivalent to the " Kekulé individuals " of aromatic chemistry. In this formula it will be seen that three of the heterocyclic corners (A, B and D) have to accommodate a double bond on the bridge and the fourth (C) an equivalent *o*-quinonoid arrangement. All the heterocyclic rings will not adapt themselves to such an arrangement with equal readiness, because the presence of the hetero-atom or atoms leads in many cases to a comparatively rigid, non-aromatic arrangement of double and single bonds. Thus pyridine is equivalent to benzene in this respect as in so many others, but *iso*oxazole (II) can only yield a compound of type (I) through the formation of a bridged form (III) :



(I.)



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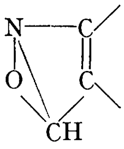

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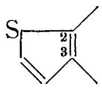

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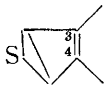

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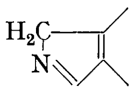
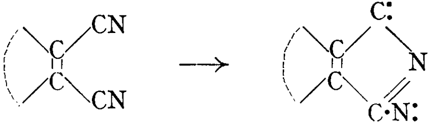


(VI.)

Moreover, in many heterocyclic rings the various pairs of *o*-carbon atoms are not equivalent. Thus the thiophen (or furan) ring may be simply fused to formula (I) in the 2 : 3-position (IV), but for fusion in the 3 : 4-position (V), bridging of the thiophen ring is necessary. In the pyrrole ring another type of adjustment is possible, for a 3 : 4-derivative can adapt itself by migration of hydrogen, as in (VI), as well as by bridging. It is reasonable to suppose that bridged structures, such as (III), will have very much lower stabilities than the corresponding unsaturated structures, such as (II). Hence there will be little possibility of resonance and a departure from the aromatic type. On these grounds it is to be expected that phthalocyanine-like compounds will not be formed from such heterocyclic rings, or if capable of existence, will be comparatively unstable.

(2) As one fundamental stage in the formation of porphyrazines is the cyclisation (VII) ⟶ (VIII), it will be affected by the ease with which the heterocyclic system yields *o*-derivatives containing a five-membered ring.

(VII.)



(VIII.)

A convenient practical guide is provided by the capacity of the corresponding *o*-dicarboxylic acids and their diamides to yield respectively anhydrides and imides. There are large differences between heterocyclic compounds in this respect. For example, as far as our present knowledge goes, anhydrides are readily formed in the pyridine, pyrazine and thiophen series, with difficulty in the pyrrole and (3 : 4-)furan group, and not at all from *iso*oxazole (3 : 4-) and triazole compounds (see table).

(3) It is obvious that the formation of porphyrazines will only proceed in the absence of side reactions. The most dangerous of these is gross thermal decomposition, but other side reactions may originate at the hetero-atom; for example, the acidity of the imino-hydrogen atom in pyrrole and particularly in triazole derivatives may lead to combination with the metallic reagents used for the preparation of the porphyrazines.

To summarise: the formation of porphyrazines from heterocyclic compounds may be expected when (i) they contain the arrangement (VII) or are capable of yielding this arrangement easily; (ii) they possess the necessary thermal stability and no disturbing reactive centre in the heterocyclic ring; and (iii) when the heterocyclic system is capable of yielding *o*-five-membered rings.

The formation of porphyrazines from the ten heterocyclic systems mentioned in the table has been investigated by the authors and Dr. J. A. Bilton. Column 2 gives the rearrangement (if any) necessary in the heterocyclic ring to accommodate porphyrazine formation. Column 3 indicates the tendency of the *o*-dicarboxylic acid of the series or its amide to yield cyclic derivatives (anhydride, imide).

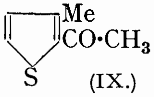
Ring.	Rearrangement.	Ortho-ring formation.
Thiophen 2 : 3	None	Easy [1]
Thionaphthen 2 : 3	None	Easy [1]
Furan 3 : 4	Bridging	Difficult [3]
Pyridine 2 : 3	None	Easy [1, 2]
Pyrazine 2 : 3	None	Easy [1]
Pyridazine 4 : 5	None	Fairly easy [1]
Pyrrole 2 : 3	None	Very difficult [4]
Pyrrole 3 : 4	Bridging or H migration	Very difficult [4]
*iso*Triazole	None	Apparently impossible [5]
*iso*Oxazole	Bridging	Apparently impossible [1]

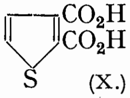
[1] See present work. [2] Engler, *Ber.*, 1894, **27**, 1788; Gabriel and Colman, *Ber.*, 1902, **35**, 2842, etc. [3] Anhydride and imide formed when the furan ring contains phenyl substituents, but not when it contains methyl substituents (Seka, *Ber.*, 1925, **58**, 1783). [4] No imides and only two anhydrides known (Piloty, *Annalen*, 1915, **407**, 5; Seka, *loc. cit.*). [5] Anhydride and imide formation apparently impossible (Fries, *Annalen*, 1927, **454**, 121, correcting earlier work by v. Pechmann, *Annalen*, 1896, **262**, 311, and Beretta, *Gazzetta*, 1926, **55**, 790).

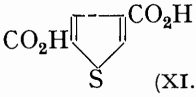
It follows from the theory outlined above that porphyrazines should be formed in the following series: thiophen (2 : 3), thionaphthen, pyridine, pyrazine, and probably pyridazine. We should not expect to obtain similar products from the corresponding furan, or *iso*oxazole derivatives, and the other three systems are doubtful.

Actually, coloured substances closely resembling phthalocyanines were obtained in the thiophen (2 : 3), thionaphthen, pyridine, and pyrazine series. Definite negative evidence was obtained in the pyrrole (3 : 4), *iso*oxazole, and *iso*triazole series. The other systems gave no positive results, but the negative results cannot be taken as conclusive, as none of the necessary *o*-dinitriles could be obtained. The present paper describes the four groups of compounds which yielded positive results. The work in the other series is described in Part X (following paper).

Preparation of Intermediates.—In the thiophen, thionaphthen and pyridine series, the general procedure followed that used for the preparation of phthalocyanines. The *o*-dicarboxylic acid, corresponding to phthalic acid, or its anhydride, was converted into the dinitrile or the *o*-cyanoamide. The starting material in the thiophen group was 3-methylthiophen; this is acetylated in the 2-position to give a ketone (IX) which can be oxidised to thiophen-2 : 3-dicarboxylic acid (X) (Demuth, *Ber.*, 1885, **18**, 3024; Gerlach, *Annalen*, 1892, **267**, 145). Actually we found that acetylation also occurred to a minor extent in the 5-position, so that the dicarboxylic acid contained the 2 : 4(= 3 : 5)-acid (XI) as impurity. Of the two acids, only the 2 : 3-acid yielded an anhydride, in agreement with the orientations given in the literature. The 2 : 3-acid was converted into the *dinitrile* by the methods described in the experimental section.


(IX.)

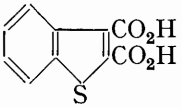

(X.)


(XI.)

Attempts to prepare thiophen-3 : 4-dicarboxylic acid from 3 : 4-dimethylthiophen and 2 : 5-dimethylthiophen-3 : 4-dicarboxylic ester from diacetylsuccinic ester were unsuccessful. The 3 : 4-series could not therefore be examined; this was unfortunate, as it would have given useful information as to the importance of the bridging effect.

The parent acid (XII) of the thionaphthen series was easily prepared from thioindoxyl, and the dinitrile obtained without much difficulty. On the other hand, although pyridine-2 : 3-dicarboxylic acid (quinolinic acid, XIII) was readily obtainable by the oxidation of 8-hydroxyquinoline, its dinitrile could not be obtained. The corresponding cyanoamide was, however, prepared and yielded phthalocyanine-like compounds.

In the pyrazine series the dinitrile was available without the intervention of the corresponding acid. Grischkevitsch-Trochimovski (*Rocz. Chem.*, 1928, **8**, 165) has shown that the tetrameride of hydrogen cyanide, reacting as diaminomaleinitrile (XIV), condenses with glyoxal to yield 2 : 3-dicyanopyrazine (XV). The structure of the product was established by hydrolysis to the corresponding acid and decarboxylation to pyrazine, although no detail was given of the method of identification of the base. In the present work we have confirmed this by hydrolysis to pyrazinemonocarboxylic acid (XVI), identified by direct comparison with material synthesised by the method of Gabriel and Sonn (*Ber.*, 1907, **40**, 4850). The formation of dicyanopyrazines in this way appears to be a general reaction of 1 : 2-diketones, comparable with the formation of quinoxalines. It occurs with diacetyl, benzil, and phenanthraquinone.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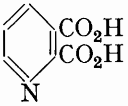
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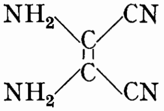
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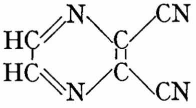
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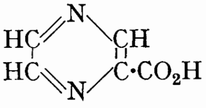
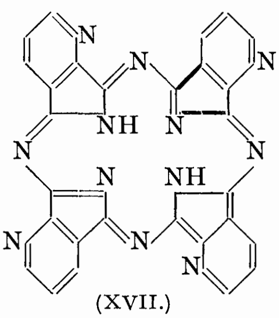

(XVI.)

Preparation of Porphyrazines.—The 2 : 3-dicyano-derivatives of thiophen, thionaphthen and pyrazine, and the 2 : 3(or 3 : 2)-cyanoamide derived from pyridine all yielded blue to green compounds when heated with suitable metallic reagents. The identification of these as the heterocyclic analogues of phthalocyanines followed from their general resemblance in physical and chemical properties, elementary composition, and absorption spectra (unpublished work by Dr. E. F. Bradbrook). The copper derivatives were prepared in all four series and also the metal-free compounds derived from thionaphthen, pyridine and pyrazine. As in the phthalocyanine group, copper was firmly held in these complexes, but magnesium was displaced by treatment with sulphuric acid and precipitation with water. The three metal-free compounds were obtained in this way.


(XVII.)

A number of difficulties were encountered in the purification of these compounds. Although fairly stable to heat, they lacked the outstanding resistance of phthalocyanines, and none could be sublimed satisfactorily. Several partly decomposed on prolonged extraction with high-boiling solvents and in only one case could a macrocrystalline product be obtained. This was probably due to the presence of structural isomerides, similar to those found among the naphthalocyanines (Bradbrook and Linstead, J., 1936, 1744). The isomerism depends upon the relative positions of the hetero-atoms and can be easily visualised for tetra-2 : 3-pyridinoporphyrazine, one form of which is shown in formula (XVII). This does not apply to the tetrapyrazinoporphyrazines, which can only exist in one form, but purification of this group was difficult owing to the formation of hydrates. As a result of these difficulties, the analytical figures were not entirely satisfactory, but showed a general agreement with the type $[R(CN)_2]_4Met.$ or $[R(CN)_2]H_2$, where R represents the heterocyclic residue and Met. a bivalent metal.

Apart from the general fall in stability, the most interesting difference between tetra-2 : 3-pyridinoporphyrazine (XVII) and phthalocyanine is that the pyridine derivative forms a *dimethiodide* and is soluble in comparatively dilute sulphuric acid. Both these reactions may be attributed to salt formation at the nitrogen atoms of the pyridine rings.

EXPERIMENTAL.

Thiophen Series.

By the method of Higson and Thorpe (J., 1906, **89**, 1462) 135 g. of ethyl cyanoacetate and 87·5 g. of acetaldehyde cyanohydrin yielded 134 g. of α-methylsuccinic acid. The following modification of Bone and Sprankling's process (J., 1899, **75**, 852) was found to be rather more convenient for the routine preparation of large quantities. The sodium compound from 143 g. of cyanoacetic ester and a solution of 28·8 g. of sodium in 350 c.c. of alcohol was treated slowly with 210 g. of ethyl α-bromopropionate. At the end of the spontaneous reaction, the mixture was heated until neutral (about ½ hour), and the methyl cyanosuccinic ester isolated in the usual way. Yield, 185 g. of a fraction, b. p. 160—165°/17 mm. The ester was boiled with 8 vols. of concentrated hydrochloric acid for 6 hours, and the product evaporated to dryness. The powdered residue was exhaustively extracted with acetone (Soxhlet). Evaporation of the extract yielded α-methylsuccinic acid, m. p. 107—109°, in 80—85% yield. The sodium salt was prepared from this acid by exact neutralisation, dried in a vacuum at 180—200°, and converted into 3-methylthiophen by fusion with phosphorus trisulphide (Volhard and Erdmann, *Ber.*, 1885, **18**, 455). With the object of improving the low and erratic yields obtained in this reaction various modifications were introduced (see table) but without much success. The best results appear to be obtained by slow initial heating. The yields given are those of material purified by refluxing over sodium and redistillation, b. p. 116—120°.

Expt.	Sodium salt, g.	P_2S_3, g.	Procedure.	Yield.
1	92	140	Rapid initial heating	9·5 g.; 18%
2	100	150	As (1) in a stream of CO_2	12 g.; 22%
3	200	250	Slow initial heating	34 g.; 30%
4	200	250	,, ,,	22 g.; 20%
5	235	295	,, ,,	37 g.; 28%
6	220	275	As (3), mixture diluted with sand	22 g.; 18%

On treatment with acetyl chloride following Demuth and Gerlach (*locc. cit.*) 3-methylthiophen gave consistently good yields (75—80%) of 2-acetyl-3-methylthiophen (IX), b. p. 98—104°/13 mm. Subsequent experiments showed this to contain a little of the 5-acetyl isomeride as impurity.

Oxidation of this ketone (cf. Gerlach, *loc. cit.*) was examined in detail, the following being a typical result: 195 g. of powdered potassium permanganate were added during 90 minutes to a mechanically stirred emulsion of 35 g. of 2-acetyl-3-methylthiophen in 2100 c.c. of water containing 280 g. of caustic soda. The reaction was complete after another hour's stirring and 2 hours' heating on the steam-bath. The liquid was filtered hot, evaporated to one-third of its bulk, acidified, and extracted six times with ether (further continuous extraction with ether yielded only oxalic acid, 4 g.). The united hand extracts yielded 24 g. of solid product, which was roughly separated by trituration with cold benzene. The soluble material (12 g.) was impure 3-methylthiophen-2-carboxylic acid (Gerlach, *loc. cit.*). The portion insoluble in benzene was separated by fractional crystallisation from water into 5 g. of thiophen-2 : 3-dicarboxylic acid (X), which formed stout prisms, m. p. 270° (Found: S, 18·5. Calc. for $C_6H_4O_4S$: S, 18·6%), and 0·8 g. of thiophen-2 : 4-dicarboxylic acid (XI), which crystallised in tufts of needles, m. p. 280° (Found: S, 18·4%). These were identified by conversion into the dimethyl esters through the silver salts. The m. p. of the 2 : 3-ester was 58° (Gerlach, *loc. cit.*, gives 60°); that of the 2 : 4-ester was 120° (Zelinsky, *Ber.*, 1887, **20**, 2017, gives 121°). The aqueous mother-liquors from these dicarboxylic acids yielded oxalic acid dihydrate (equiv., 63; m. p. and mixed m. p. 102°).

The effect of minor variations in the experimental conditions of the oxidation on the yield and nature of the products is shown in the table. The ease with which the monocarboxylic acid is formed without oxidation of the methyl group is indicated by experiment (3).

Expt.	Ketone, g.	Alkali, g.	Water, l.	Permanganate, g.	Yield, monocarboxylic acid, g.	Yield, dicarboxylic acid, g.
	5	4	0·3			
1	35	280	2·1	195	12	5·8
2	32	265	3	176	10·2	6
3	96	600	6	516	56	1
4	45	360	3·6	246	20	8
5	32	350	2	176	7	3

3-Methylthiophen-2-carboxylic acid, when once formed, resisted all attempts at oxidation to the dicarboxylic acid, the only isolated product being oxalic acid.

Oxidation of Thionaphthen.—Attempts were made to prepare thiophen-2 : 3-dicarboxylic acid by the direct oxidation of thionaphthen. Thioindoxyl was separated from the commercial melt of phenylthioglycollic-*o*-carboxylic acid by acidification with concentrated hydrochloric acid at 90° in an atmosphere of carbon dioxide. The product was reduced with zinc dust in boiling acetic acid, and the thionaphthen isolated by neutralisation and distillation in steam, m. p. 32° (cf. Friedländer, *Ber.*, 1908, **41**, 230). Thionaphthen was oxidised under the conditions tabulated below. The liquid was filtered, cleared with sulphur dioxide, and extracted exhaustively with ether.

Thionaphthen, g.	Permanganate, g.	Alkali.	Water, c.c.	Conditions.
7	47	60 g. NaOH	500	2 Hours at b. p.
5	34	50 g. NaOH	500	4 Days at 80° with 500 c.c. of acetone.
5	34	None	500	4 Days at 80°.
7	45	60 g. NaOH	700	2 Weeks at 35°.
4·5	35	9 g. $CaCO_3$	900	Compare the preparation of pyridine-2 : 3-dicarboxylic acid, p. 918.

In no case was any organic acid, soluble in ether, isolated; nor could the presence of sulphonic or sulphinic acid be detected. Sulphate was present in the original oxidation product, before the addition of sulphur dioxide. Hence such thionaphthen as is not recovered unchanged with the manganese dioxide is completely oxidised under these experimental conditions.

Derivatives of Thiophen-2 : 3-dicarboxylic Acid.—The pure acid (4·5 g.) was refluxed for 30 minutes with 16 c.c. of acetic anhydride, the cooled product poured into 500 c.c. of water, and the precipitate of *anhydride* filtered off, dried, and crystallised from benzene; m. p. 140°, yield 3·6 g. (Found : S, 20·4. $C_6H_2O_3S$ requires S, 20·7%). The anhydride could also be made by similar treatment of the mixed dibasic acids (insoluble in benzene) obtained from the oxidation of acetyl-3-methylthiophen. The 2 : 4-acid separated slowly from the residual solution after removal of the 2 : 3-anhydride. This difference confirms the orientation of the carboxyl groups in these acids. The anhydride sublimed in poor yield when the 2 : 3-acid was heated in a current of nitrogen or, better, at 2 mm. pressure. It was not formed by the action of a mixture of phosphorus pentachloride and oxychloride on the acid.

Thiophen-2 : 3-dicarboxylic acid (7·5 g.) was refluxed for 18 hours with 25 c.c. of thionyl chloride and 17 c.c. of dry benzene. The excess of reagent was removed under diminished pressure, the residual acid chloride dissolved in 100 c.c. of dry benzene, and the solution saturated with dry ammonia for ½ hour. The precipitated *diamide* crystallised from water in needles, m. p. 228°. Yield, 4 g. (53%) (Found : N, 16·5. $C_6H_6O_2N_2S$ requires N, 16·5%). Acidification of the mother-liquor from the diamide yielded 2 g. of a white flocculent precipitate of the corresponding amic acid (2 : 3- or 3 : 2-), m. p. 238°, soluble in sodium bicarbonate solution. The amic acid on dehydration at 230—240° with phosphoric oxide yielded 1 g. of the *imide* of thiophen-2 : 3-dicarboxylic acid as a crystalline sublimate, m. p. 204° (Found : N, 9·0. $C_6H_3O_2NS$ requires N, 9·1%). The structure of this followed from the fact that it gave the diamide (m. p. 228°) in good yield after standing overnight with aqueous ammonia (*d* 0·880). A mixture of diamide and amic acid was also formed, but in worse yield, by treating the anhydride with phosphorus pentachloride, removing the phosphorus oxychloride, and treating the acid chloride in the manner described above.

An intimate mixture of 9 g. of the diamide and 15 g. of phosphoric oxide was heated in a special apparatus, which was found convenient for the distillation and sublimation of unstable solids. This consisted of a vertical tube, fitted with a wide horizontal side-arm, and enclosed in a fused-on outer jacket containing a suitable heating liquid. At a bath temperature of 180—190° and 3 mm. pressure, the above mixture gave a distillate, b. p. 130—135°, which immediately solidified in the side-arm. The crude product (3·2 g., m. p. *ca.* 120°) was 2 : 3-*dicyanothiophen* contaminated with about 20% of imide (Found : N, 18·5%). The mixture was kept overnight in aqueous ammonia (*d* 0·880), and the solid filtered off and extracted with acetone. Evaporation of the acetone extract left the dinitrile, which formed needles from light petroleum, m. p. 140° (Found : N, 20·3. $C_6H_2N_2S$ requires N, 20·9%). Dehydration of the diamide with acetic anhydride also yielded crude dinitrile, but in worse yield.

The dinitrile (1·7 g.) was heated at 230—250° with 1·4 g. of cuprous chloride for about 10 minutes, the mixture becoming solid. The product was powdered and exhaustively extracted with boiling alcohol. The blue residue was dusted into concentrated sulphuric acid, and the brown solution filtered through asbestos and poured on ice. The greenish-blue precipitate was washed and dried (1·1 g.) and twice crystallised from chloronaphthalene by the usual technique. This procedure was wasteful, as even exhaustive extraction left a considerable residue (which gave a fine blue solution in quinoline) and as a good deal of the soluble pigment failed to separate from the chloronaphthalene.

Copper tetra-2 : 3-*thiophenoporphyrazine* separated as a greenish-blue powder with a faint purple lustre (Found : C, 47·7; H, 1·8; S, 19·4; Cu, 9·6. $C_{24}H_8N_8S_4Cu$ requires C, 48·0; H, 1·7; S, 21·3; Cu, 10·6%). The substance was greener than free phthalocyanine and resembled zinc phthalocyanine hydrochloride. It could not be sublimed under the conditions normally used for phthalocyanines. A similar compound appeared to be formed from 2 : 3-dicyanothiophen and metallic copper, but the nitrile gave no obvious signs of pigment formation when heated with sodium amyloxide, litharge, or magnesium.

3 : 4-*Thiophen Series*.—(*a*) Ethyl methylcyanosuccinate (160 g.) was methylated following Bone and Sprankling (*loc. cit.*), and the dimethylated ester (133 g.) hydrolysed with 6 volumes of boiling concentrated hydrochloric acid for 20 hours. The solution was evaporated to dryness, and the αβ-dimethylsuccinic acid extracted with acetone. Dry distillation of a mixture of 195 g. of the sodium salt of this acid (dried at 200°) and 245 g. of phosphorus trisulphide in a stream of carbon dioxide yielded 83 g. of crude dimethylthiophen. This was left in contact with sodium hydroxide for 15 hours, refluxed over sodium for 6 hours, and fractionated. Yield of 3 : 4-dimethylthiophen, b. p. 145—148°, 50 g. (compare Zelinsky, *Ber.*, 1888, **21**, 1836). Oxidation of this substance with alkaline permanganate under a variety of conditions yielded mainly oxalic acid, a small amount of 3-methylthiophen-4-carboxylic acid, and no thiophen-3 : 4-dicarboxylic acid.

(*b*) Diacetylsuccinic ester (Knorr, *Ber.*, 1894, **27**, 1155) yielded only a black pitch when refluxed with 1·5 parts of phosphorus pentasulphide in 5 parts of toluene for one hour. When 5 g. of the ester were refluxed for 90 minutes with 1·7 g. of phosphorus pentasulphide in 25 c.c. of anhydrous benzene, some hydrogen sulphide was evolved, but after filtration of the unattacked sulphide, evaporation of the solvent led to a good recovery of the ester and no other isolable product.

Thionaphthen Series.

Thionaphthenquinone (33 g., m. p. 118—119°) was prepared from thioindoxyl (43 g.) essentially by Mayer's method (*Annalen*, 1931, **488**, 259) and was converted into thionaphthen-2 : 3-dicarboxylic acid (XII) following Friedländer (*Ber.*, 1908, **41**, 227). Yield 75% of needles, m. p. 255°. The acid gave an excellent yield of anhydride, m. p. 173°, when boiled for ½ hour with 3 volumes of acetic anhydride (cf. Mayer, *loc. cit.*).

The anhydride (15 g.) was heated with phosphorus pentachloride (12 g.) for 6 hours at 150—160°. The acid chloride (m. p. 70—72°) separated partly on standing and partly after removal of phosphorus oxychloride. Yield, 18 g. (90%). It was dissolved in anhydrous benzene and treated with dry ammonia gas. The white precipitate of *thionaphthen*-2 : 3-*dicarboxyamide* was crystallised from water. Yield 2 g., m. p. 204—205° (Found : N, 12·9. $C_{10}H_8O_2N_2S$ requires N, 12·7%). Acidification of the aqueous mother-liquor from this yielded 2 g. of a white solid, presumably the amic acid. This on distillation with phosphoric oxide yielded *thionaphthen*-2 : 3-*dicarboxyimide*, which crystallised from acetic acid in small plates, m. p. 240° (Found : N, 7·2. $C_{10}H_5O_2NS$ requires N, 6·9%). When treated with an excess of aqueous ammonia (*d* 0·880), the imide gave a quantitative yield of the diamide, m. p. 204°. Experiments on the preparation of the acid chloride from the acid and thionyl chloride were unsatisfactory. The principal product was the anhydride, m. p. and mixed m. p. 173°. Preliminary experiments on the preparation of the imide by melting the anhydride with ammonium carbonate and with urea also gave unpromising results.

Thionaphthen-2 : 3-dicarboxyamide (2 g.) was refluxed for 1 hour with 6 c.c. of acetic anhydride (6 mols.). The product was cooled and poured into water. The precipitated 2 : 3-*dicyanothionaphthen* (1·5 g.) was crystallised from alcohol to a constant m. p. of 148° (1·2 g.) (Found: N, 14·9. $C_{10}H_4N_2S$ requires N, 15·2%). Similar yields of 80—85% were obtained on a larger scale. When 5 g. of the diamide were dehydrated by 30 minutes' refluxing with 5 c.c. of acetic anhydride and an equal volume of acetic acid, the product (4·5 g.) was 2(or 3)-*cyanothionaphthen*-3(or 2)-*carboxyamide*, which crystallised from alcohol in long needles, m. p. 192—194° (Found: N, 13·7. $C_{10}H_6ON_2S$ requires N, 13·9%). This yielded green pigments when heated with cuprous chloride, reduced copper and, less readily, with magnesium. An intimate mixture of 1 g. of the diamide and 1 g. of phosphoric oxide was heated at *ca.* 1 mm. in the special apparatus already described. Reaction commenced at about 220° and the bath temperature was maintained at 230—240° until nothing further sublimed and the charred residue began to swell; 0·4 g. (*ca.* 70%) of solid was removed from the side-arm. This melted at about 195° and was a mixture of dinitrile and imide (Found: N, 9·8%). Separation was difficult, treatment with ammonia (cf. p. 917) being unsatisfactory. Repeated extraction with cold ether, alcohol, or benzene led to an accumulation of imide in the less soluble fraction and this was finally crystallised from acetic acid; it then melted at 238° and was identical with that already described. The purest dinitrile which could be isolated from the soluble portion melted at 140—145° and contained 14·0% of nitrogen (Calc., 15·2%).

Tetra-2 : 3-*thionaphthenoporphyrazines.*—A mixture of 1 g. of 2 : 3-dicyanothionaphthen and 0·5 g. of cuprous chloride was heated at 240—250° for 30 minutes, and the product cooled, powdered, and exhaustively extracted with alcohol to remove unreacted nitrile. The dark green residue was dissolved in concentrated sulphuric acid (blue solution), precipitated in the usual way, washed with water until free of acid, and finally washed with alcohol. The product (0·5 g.) was extracted with chloronaphthalene (green solution), from which it separated as a dull green powder with a faint purple lustre. The colour was slightly duller than that of 1 : 2-naphthalocyanine (Found for once crystallised material: C, 58·1; H, 2·3; N, 12·9; S, 15·4. Found for twice crystallised material: C, 58·7; H, 1·8; N, 12·3; S, 15·2. $C_{40}H_{16}N_8S_4Cu$ requires C, 60·0; H, 2·0; N, 14·0; S, 16·0. $C_{40}H_{15}N_8ClS_4Cu$ requires C, 57·5; H, 1·9; N, 13·4; S, 15·3%). The last of these sets of figures corresponds with the substitution of chlorine for one nuclear hydrogen as in copper monochlorophthalocyanine (Dent and Linstead, J., 1934, 1027). As in the thiophen series, the extraction was inefficient and the product from sulphuric acid treatment appeared to be a mixture of substances of closely similar type. A portion was undissolved even by prolonged extraction with chloronaphthalene at 260°, but dissolved in sulphuric acid and yielded a green precipitate on dilution. A considerable amount of the soluble portion failed to separate from the chloronaphthalene. A similar preparation using reduced copper in place of cuprous chloride gave a product indistinguishable from the above (Found: C, 57·8; H, 1·9; N, 12·2; S, 15·1%). Reaction between the 2 : 3-cyanoamide (m. p. 193°, 2 g.) and reduced copper (1·25 g.) proceeded vigorously at 240—250°. The dark green product, worked up as before, was purified through sulphuric acid (yield, 1·3 g.) and showed a similar lack of homogeneity when extracted with chloronaphthalene.

2 : 3-Dicyanothionaphthen reacted smoothly with aluminium chloride at 250° to give a dark green pigment, soluble in chloronaphthalene and slightly soluble in alcohol (green solution). The solution in concentrated sulphuric acid was dark olive-green and yielded a green precipitate on dilution, the colour of which was unchanged by alkali. The dinitrile reacted readily with etched magnesium at 250° to give a dark green pigment partly soluble in ether, like α-magnesium 1 : 2-naphthalocyanine (Bradbrook and Linstead, *loc. cit.*). Three days' extraction with ether (Soxhlet) separated the product into a soluble portion (ash, 4·9%. Calc., for magnesium tetrathionaphthenoporphyrazine, 5·3%) and an insoluble portion (ash, 4·5%) which were indistinguishable in appearance. The insoluble portion dissolved in sulphuric acid with an olive-green colour, and the solution gave a dark green precipitate of metal-free compound on dilution (ash, 0·4%).

Pyridine Series.

Pyridine-2 : 3-dicarboxylic (quinolinic) acid (XIII) was prepared by the oxidation of quinoline (compare G. P. 414,072) and, better, of 8-hydroxyquinoline (Sucharda, *Ber.*, 1925, **58**, 1727). The direct oxidation of the base gave indifferent yields in spite of a large number of modifications. The following experiments are typical. (*a*) 10 G. of quinoline were gradually added to a mechanically stirred solution of 82 g. of potassium permanganate in 2 l. of water containing 20 g. of calcium carbonate. After 15 hours' stirring, the solution was filtered, evaporated to a syrup, acidified with nitric acid, neutralised, and treated with silver nitrate until there was no further precipitate. The precipitate was washed, dried (35 g.), and refluxed for 48 hours with 30 c.c. of ethyl iodide and 600 c.c. of dry ether. The ester was fractionated into 5 g. of ethyl oxalate, b. p. 80°/15 mm., and 4 g. of ethyl quinolinate, b. p. 170—180°/15 mm. The ethyl oxalate was identified by conversion into oxamide (Found : N, 32·1. Calc., 31·9%). The use of barium carbonate in place of calcium carbonate gave a similar result. Variation in the concentration had little effect, and in an experiment on a much larger scale (500 g. of quinoline) the proportion of ethyl oxalate to quinolinate in the product rose to *ca.* 10 : 1. (*b*) Process (*a*) was followed except that lead nitrate was used in place of silver nitrate. The powdered dry lead salt (33 g.), suspended in 100 c.c. of water, was treated at 60° with a rapid stream of hydrogen sulphide. The lead sulphide was filtered off and washed thoroughly with boiling water. The filtrate yielded 5 g. of oxalic acid on evaporation to small bulk, and 1 g. of quinolinic acid separated from the washings. (*c*) By Sucharda's process (*loc. cit.*), 200 g. of 8-hydroxyquinoline yielded an equal weight of quinolinic acid, which formed fine needles from acetic acid, m. p. 230° (decomp.); 14 g. of this, through the silver salt, yielded 11 g. of the diethyl ester, b. p. 170°/10 mm. The ester was more conveniently prepared on a larger scale by refluxing the *carefully dried* acid with 10 volumes of absolute alcohol for 6 hours in a current of dry hydrogen chloride. It was isolated in the usual manner, b. p. 175°/15 mm.; yield, 70%.

Ethyl quinolinate (47 g.) was shaken with an excess of aqueous ammonia, saturated at 0°, for 24 hours. Pure quinolinamide (25 g.) separated in white needles, m. p. 209° in agreement with Engler (*Ber.*, 1894, **27**, 1788). The yield was slightly lower if ammonia (*d* 0·880) was used. The methyl ester gave the same result. The corresponding imide was prepared by Sucharda's method (*loc. cit.*) and had m. p. 233° after crystallisation from acetic acid or sublimation.

20 G. of quinolinamide were refluxed for 2 hours with 12 c.c. of acetic anhydride and 11 c.c. of acetic acid. On cooling, the solution deposited 15 g. of 2(or 3)-*cyanopyridine*-3(or 2)-*carboxyamide*, m. p. 255—260° after crystallisation from water (Found : C, 56·9; H, 3·8; N, 28·4. $C_7H_5ON_3$ requires C, 57·2; H, 3·4; N, 28·6%). This substance readily formed blue pigments when heated with metallic reagents. (It is possible that it is actually the cyclic isomeride, iminoquinolinimide.) When the dehydration of the diamide was carried out with acetic anhydride alone, the yield of cyanoamide was lower and the mother-liquors contained a substance, m. p. 150°, with a comparatively low nitrogen content. This was probably the *acetyl* derivative of quinolinimide; the analytical figures indicate that it was not quite pure (Found : C, 56·2; H, 3·2; N, 15·9. $C_9H_6O_3N_2$ requires C, 56·8; H, 3·2; N, 14·7%). It gave no pigments when heated with metallic reagents. A similar product was formed by the action of acetic anhydride on the cyanoamide.

The dinitrile of quinolinic acid could not be obtained by " chemical " dehydration of the diamide or cyanoamide (see below), but was obtained in very poor yield by the following catalytic process suggested by the general method of Reid (*J. Amer. Chem. Soc.*, 1916, **38**, 2128; 1931, **53**, 321). 5 G. of the diamide were placed in one end of a horizontal hard glass tube, the bulk of which was packed with silica gel. The catalyst was heated to 320—350°, and the diamide sublimed in a stream of dry ammonia gas. There was gross decomposition and only 0·4 g. of solid product was isolated, m. p. about 100°, which readily yielded a blue pigment when heated with copper and cuprous chloride. After crystallisation from benzene–light petroleum this melted at 130° and was nearly pure 2 : 3-*dicyanopyridine* (Found : N, 31·5. $C_7H_3N_3$ requires N, 32·6%). When the diamide was heated at 230° with phosphoric oxide, the sublimed product was crude imide, m.p. *ca.* 230° (Found: N, 21·0%). A similar result was obtained by heating the cyanoamide with phosphoric oxide at 270°, the product having m. p. *ca.* 240° (Found : N, 19·8. Calc. for $C_7H_4O_2N_2$: N, 18·9%).

Tetrapyridinoporphyrazines.—A mixture of 5 g. of the cyanoamide and 1 g. of etched magnesium turnings was heated with stirring to 270—280° during 10 minutes. An intense purple reflex rapidly developed. The material was cooled, powdered, stirred with dilute hydrochloric acid to remove free magnesium, washed, and dried. The magnesium compound (4·8 g.) was then dissolved in concentrated sulphuric acid, and the solution poured on ice. The blue precipitate was washed, dried (1·2 g.), and crystallised from chloronaphthalene in an extractor.

Tetra-2 : 3-*pyridinoporphyrazine* (XVII) formed fine blue needles with a purple reflex (0·8 g.) (Found : C, 64·5; H, 2·8; N, 31·6. $C_{28}H_{14}N_{12}$ requires C, 64·8; H, 2·7; N, 32·4%). The rubbing was rather bluer than that of phthalocyanine, and about the same shade as that of cobalt phthalocyanine. The solution in chloronaphthalene was greenish-blue, and in sulphuric acid bright green. The compound was insoluble in alcohol and other low-boiling solvents. Sublimation at low pressures gave a very poor yield of crystalline product. The elimination of metal from the magnesium derivative was improved by using dilute acids. 50 and 75% Sulphuric acid (by vol.) gave a 32% recovery of tetrapyridinoporphyrazine. The magnesium pigment was completely dissolved by 10 volumes of 25% sulphuric acid (by vol.), and dilution precipitated tetrapyridinoporphyrazine in 38% yield. No solid salts with sulphuric acid could be isolated. The solubility in relatively dilute acids contrasts with that of phthalocyanine, which only dissolves in sulphuric acid containing about 75% of acid by volume.

1 G. of tetrapyridinoporphyrazine was heated for 4 hours at 160° with 5 c.c. of methyl iodide. The solid product (1·2 g.) was rather greener than the parent substance and after extraction with pyridine and alcohol corresponded approximately to a *dimethiodide* (Found: I, 32·7. $C_{28}H_{14}N_2,2CH_3I$ requires I, 31·4%). The iodine was readily removed by boiling aqueous alkali.

A blue copper derivative was prepared both by heating 2 : 3-dicyanopyridine with cuprous chloride at 240° and from quinolinamide, copper and ammonium aminosulphonate at 270°, but it was found impossible to obtain it in a state of analytical purity. In the latter process, 10 g. each of aminosulphonic acid and ammonium carbonate were fused together at 140° until a clear melt was obtained; 2·5 g. of quinolinamide and 0·7 g. of reduced copper were then added, and the temperature raised to 270° until the mass was solid (15 minutes). The product was cooled and extracted successively with boiling water and boiling alcohol, after which a yield of 65% (calc. on the diamide) of a blue powder remained. Purification of this through concentrated sulphuric acid in the usual way was unsatisfactory, as the precipitated material formed a fine suspension which could not be filtered. The copper compound was soluble in 50% sulphuric acid, but use of dilute acids and neutralisation of the suspensions were alike without effect. Crystallisation of the crude pigment from quinoline and chloronaphthalene gave difficulty owing to the low solubility. This necessitated a long period of extraction which led to considerable decomposition. Satisfactory analyses could not therefore be obtained, but from the general behaviour there was no doubt that a considerable proportion of the desired copper derivative was present. The copper compound prepared from the dinitrile gave similar results.

Pyrazine Series.

Diaminomaleinitrile (XIV) * (compare Grischkevitsch-Trochimovski, *loc. cit.*).—After preliminary experiments, consistent yields were obtained as follows: 238 g. of hydrogen cyanide were distilled through a tube of calcium chloride into a strong flask, 1 g. of potassium cyanide was added, and the mixture left corked in the open air for 3—4 days at a mean temperature of 10°. The liquid was then decanted into a fresh vessel, and the process repeated, the last traces of liquid being allowed to evaporate. The rate of polymerisation was at first about 6 g. per day, but later fell to less than half this. The combined yield of solid " azulmin " was 190 g. (80%), which on Soxhlet extraction with ether for 3 days gave 33 g. (17%) of crude tetrameride. If the polymerisation was allowed to proceed without periodic decanting, more of the higher polymerides appeared to be formed. 5 G. of the crude tetrameride on crystallisation from water (charcoal) gave 3·8 g. of diaminomaleinitrile in reddish needles, m. p. 179° (decomp.) (Found: C, 44·3; H, 3·6; N, 50·5. Calc. for $C_4H_4N_4$: C, 44·4; H, 3·7; N, 51·9%). For the following preparations the crude tetrameride could be used.

2 : 3-Dicyanopyrazine (XV), prepared from the tetrameride and glyoxal, following Grischkevitsch-Trochimovski, formed colourless feathery needles from water, m. p. 132° (Found: C, 55·4; H, 1·6; N, 43·2. Calc. for $C_6H_2N_4$: C, 55·4; H, 1·5; N, 43·1%). 1 G. of 2 : 3-dicyanopyrazine was refluxed for 18 hours with 5 c.c. of concentrated hydrochloric acid. The product was evaporated to dryness and extracted with acetone. The extract yielded 0·6 g. of pyrazinemonocarboxylic acid (XVI), which formed needles, m. p. 221° (decomp.), after crystallisation from water (Found: C, 48·7; H, 3·3. Calc. for $C_5H_4O_2N_2$: C, 48·4; H, 3·2%). The mother-liquors from this acid yielded a silver salt, from which the same acid was regenerated; there was no sign of the presence of the dicarboxylic acid. 1 G. of 2 : 3-dicyanopyrazine was treated with 10 c.c. of 10% aqueous caustic potash and sufficient alcohol for solution. After 36 hours' refluxing, the alcohol was removed, and the product converted into the silver salt (3 g.), from which 0·8 g. of crude pyrazine-2 : 3-dicarboxylic acid was liberated. As this was difficult to purify by crystallisation, it was decarboxylated by sublimation at 200° into the monocarboxylic acid, m. p. 221° (decomp.) after crystallisation from water. The identity of both these samples of pyrazinemonocarboxylic acid was confirmed by mixed m. p. determinations with authentic material (m. p. 221°, decomp.) prepared from quinoxaline through pyrazinedicarboxylic acid by the method of Gabriel and Sonn (*loc. cit.*).

Substituted Dicyanopyrazines.—A mixture of 0·65 g. of the crude tetrameride, 1 g. of diacetyl,

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* The name is used for convenience, although there is evidence that the compound usually reacts as the imino-modification (private communication from Dr. L. E. Hinkel).

0·5 c.c. of glacial acetic, 10 c.c. of water and 10 c.c. of alcohol was heated at 80° for 30 minutes. After the addition of charcoal, the solution was boiled and filtered. The filtrate deposited 2 : 3-*dicyano*-5 : 6-*dimethylpyrazine* in light yellow plates, m. p. 166° (Found : C, 60·7; H, 4·1. $C_8H_6N_4$ requires C, 60·8; H, 3·8%).

To a solution of 0·5 g. of the crude tetrameride, 0·6 c.c. of hydrochloric acid, and 0·5 g. of sodium acetate in 10 c.c. of water on the water-bath, were added 1 g. of benzil and enough alcohol to clear the solution. After 30 minutes' heating, the filtered solution deposited long needles of 2 : 3-*dicyano*-5 : 6-*diphenylpyrazine* (1·5 g.), which formed small plates from alcohol, m. p. 245° (Found : C, 76·3; H, 3·7. $C_{18}H_{10}N_4$ requires C, 76·6; H, 3·6%).

A solution of 1 g. of phenanthraquinone, 0·5 g. of the crystallised tetrameride, and 0·5 c.c. of acetic acid in alcohol was refluxed for 2 hours. 2 : 3-*Dicyanophenanthra*(9′ : 10′ : 5 : 6)*pyrazine* (1 g.) separated partly in the hot, partly on cooling, and crystallised from benzene in golden needles, m. p. 320° (Found : C, 77·5; H, 3·2. $C_{18}H_8N_4$ requires C, 77·1; H, 3·0%).

Tetrapyrazinoporphyrazines.—2 G. of 3 : 4-dicyanopyrazine were heated with 1 g. of cuprous chloride. A blue colour developed at 130°, the internal temperature rose rapidly to *ca.* 250°, and hydrogen chloride was evolved. The powdered product was washed with aqueous ammonia, water, and alcohol, and (2·3 g.) dissolved in concentrated sulphuric acid. The deep blue solution was filtered, and the pigment precipitated with ice in the usual way. Yield, 1·5 g. of *copper tetrapyrazinoporphyrazine tetrahydrate* as a blue solid with a purple lustre. Chlorine and sulphur were absent. After drying in a desiccator over calcium chloride (Found : C, 44·1, 44·2; H, 1·9, 2·3; N, 35·3; Cu, 9·8. $C_{24}H_8N_{16}Cu,4H_2O$ requires C, 43·9; H, 2·4; N, 34·1; Cu, 9·7%), this yielded the stable *trihydrate* after drying in a vacuum over sulphuric acid (Found : C, 45·0; H, 2·3; Cu, 9·8. $C_{24}H_8N_{16}Cu,3H_2O$ requires C, 45·2; H, 2·2; Cu, 10%). The last molecule of water was held very firmly. The tetrahydrate lost 5·67% in weight at 150° (calc. for $2H_2O$, 5·6%), and 8·54% at 200° (calc. for $3H_2O$, 8·46%). The residue then had C, 47·1; H, 1·8; Cu, 11·0%. There was very little loss at 200° in a vacuum and the final product was the *monohydrate* (Found : C, 47·8; H, 1·7; Cu, 10·6. $C_{24}H_8N_{16}Cu,H_2O$ requires C, 47·8; H, 1·7; Cu 10·6%). The monohydrate reverted to the trihydrate in the air of the laboratory (Found : C, 45·7; H, 2·2; N, 35·2; Cu, 10·2%. Calc. for $C_{24}H_8N_{16}Cu,3H_2O$: C, 45·2; H, 2·2; N, 35·2; Cu, 10·0%. Found : gain in weight, 5·1. Calc. for $2H_2O$, 5·6%). The copper analyses enumerated above were calculated from the residue left after combustion. An estimation on the trihydrate by ashing in an open crucible gave a value 10·54% Cu, which was checked by dissolving the ash in nitric acid and estimating the metal volumetrically (Found : Cu, 10·45%). Other preparations of the trihydrate gave products with identical analytical figures.

The trihydrate was practically insoluble in pyridine, quinoline and chloronaphthalene. Attempts to crystallise it by prolonged extraction with quinoline led to decomposition. All forms of copper tetrapyrazinoporphyrazine were blue with a purple reflex, and none could be sublimed. The trihydrate was decolorised on treatment with nitric acid, acid permanganate, or acid ceric sulphate, but only oxalic acid and no pyrazine derivatives could be isolated from the solutions so obtained.

3 : 4-Dicyanopyrazine (4 g.) was heated with excess of etched magnesium at 200° for several hours. The blue solid which slowly formed was washed with dilute acid, water and alcohol and dried in a vacuum over calcium chloride (yield, 2·9 g.) (Found in two different samples : C, 53·4, 54·0; H, 2·3, 2·3; ash 0·6, 1·1. $C_{24}H_{10}N_{16}$ requires C, 55·2; H, 1·9%). The analyses indicated that elimination of the metal was incomplete. The pigment gave a greenish-blue solution in concentrated sulphuric acid, which, on pouring on ice, yielded *tetrapyrazinoporphyrazine tetrahydrate* as a blue powder (Found : C, 48·5; H, 3·0. $C_{24}H_{10}N_{16},4H_2O$ requires C, 48·5; H, 3·0%). Magnesium could not be eliminated completely from the crude magnesium compound by washing with concentrated hydrochloric acid. The pigment, both before and after treatment with sulphuric acid, could not be crystallised from pyridine, quinoline, and chloronaphthalene (in which it was very slightly soluble in the hot); neither could it be sublimed. Similar coloured substances were obtained by heating dicyanopyrazine with calcium ethoxide, stannous chloride, aluminium chloride, reduced copper, cupric chloride, and zinc chloride. The dicyanopyrazines derived from diacetyl, benzil and phenanthraquinone also gave coloured solids with these reagents, which were not examined in detail. The colours changed from blue to green with increasing molecular weight.

We thank Imperial Chemical Industries, Ltd., for grants and gifts of chemicals.

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[*Received, April* 15*th*, 1937.]
