

of spectral bands,^{5,12-14} isotope-exchange reactions,¹⁵⁻¹⁷ and replacement reactions.^{5,16,18} In a study of the relative ease of demetallation of metal phthalocyanines with acid Berezin¹⁵ concluded that this method also constituted a valid criterium for determining relative stabilities. Caughey and Corwin⁵ have applied this method to metalloporphyrins on a semiquantitative basis by measuring their rates of demetallation. The various methods agree remarkably well and give a stability order $\text{Pt}^{\text{II}} > \text{Pd}^{\text{II}} > \text{Ni}^{\text{II}} > \text{Co}^{\text{II}} > \text{Ag}^{\text{II}} > \text{Cu}^{\text{II}} > \text{Fe}^{\text{II}} > \text{Zn}^{\text{II}} > \text{Mg}$ for a given porphyrin¹¹ or phthalocyanine.¹⁵

The present work developed from an extension of earlier studies^{19,20} on the reduction of porphyrins. A number of metal-amine systems were investigated, including lithium in ethylenediamine, which has recently found application as a reducing agent.²¹ When lithium was added to a solution of iron octaethylporphin in boiling ethylenediamine the central iron atom was replaced by lithium. Since the resulting lithium complex is readily converted into the metal-free porphyrin, this represents a demetallation reaction under relatively mild, basic conditions. A number of other metalloporphyrins behaved analogously and it was decided to investigate the reaction systematically.

Accordingly we prepared a number of metal derivatives of α etioporphyrin I (II) and *meso*-tetraphenylporphin (III; R = Ph). Their copper, cobaltous, and nickel derivatives were readily prepared by standard methods. Tin α etioporphyrin I was prepared by Corwin's method;²² the crude product was the dichloride, and not the diacetate as reported earlier.^{22,23} The preparation of platinum and palladium *meso*-tetraphenylporphin derivatives has been described by Thomas and Martell¹⁴ who obtained low yields of impure products which had to be subjected to lengthy purification procedures. We found that palladium and platinum porphyrin complexes were readily obtained in good yield and high purity by treatment of the porphyrin in an inert solvent with the complex salts $\text{PdCl}_2(\text{PhCN})_2$ (IV) and $\text{PtCl}_2(\text{PhCN})_2$ (V), respectively. Benzene was used as solvent for salt (IV), and benzonitrile for (V) because of its low solubility in benzene. This method was applied to the preparation of palladium α etioporphyrin I,²⁴ platinum *meso*-tetraphenylporphin,¹⁴ and the hitherto unknown platinum α etioporphyrin I and palladium octaethylchlorin (VI). Solutions of platinum octaethylchlorin, and the palladium and platinum *a*-tetrahydro-octaethylporphin²⁰ derivatives were prepared similarly but not isolated in the solid state. Application of the method to palladium *meso*-tetraphenylporphin afforded a green material which is at present under investigation, but the desired product could be obtained in fair yield with palladous chloride in boiling benzonitrile. The use of the complexes (IV) and (V) for the preparation of metalloporphyrins appears to be a general reaction and is particularly valuable for the synthesis of complexes of the unstable hydroporphyrins which are not accessible by other methods.

Solutions of dilithioporphyrins were required for comparison of their spectral characteristics with those of the products of the lithium-ethylenediamine reaction and their preparation was accordingly undertaken. The literature methods involve treatment of the porphyrin in pyridine with an alcoholic solution of lithium hydroxide⁶ or methoxide.¹⁶ We found these methods difficult to reproduce but discovered that the dilithioporphyrins were readily formed when a benzene solution of the porphyrin was treated with a solution of phenyl- or butyl-lithium, or with lithium in ethylenediamine.

¹² Williams, *Chem. Rev.*, 1956, **56**, 299.

¹³ Thomas and Martell, *Arch. Biochem. Biophys.*, 1958, **76**, 286.

¹⁴ Thomas and Martell, *J. Amer. Chem. Soc.*, 1959, **81**, 5111.

¹⁵ Berezin, (a) *Dokl. Akad. Nauk S.S.S.R.*, 1961, **141**, 353; (b) *Zhur. fiz. Khim.*, 1962, **36**, 494.

¹⁶ Barnes and Dorough, *J. Amer. Chem. Soc.*, 1950, **72**, 4045.

¹⁷ Stranks and Wilkins, *Chem. Rev.*, 1957, **57**, 743.

¹⁸ Corwin and Melville, *J. Amer. Chem. Soc.*, 1955, **77**, 2755.

¹⁹ Eisner, Lichtarowicz, and Linstead, *J.*, 1957, 733.

²⁰ Eisner, *J.*, 1957, 3461.

²¹ Gaiffe, *Chimie et Industrie*, 1962, **88**, 37, and references cited therein.

²² Corwin and Collins, *J. Org. Chem.*, 1962, **27**, 3060.

²³ Fischer and Neumann, *Annalen*, 1932, **494**, 240.

²⁴ Johnson, Kay, Markham, Price, and Shaw, *J.*, 1959, 3416.

It was found that demetallation* of metalloporphyrins with lithium-ethylenediamine is dependent on a number of factors, including the nature of the metal and of the porphyrin, the amount of lithium added, concentration, and temperature. Systematic investigations were carried out under conditions of constant temperature and concentration in order to determine the effect of the central metal atom on the amount of lithium required for complete demetallation (see Table 1). This amount is far in excess of the stoicheiometric

TABLE I.
Demetallation with lithium metal in ethylenediamine.

Metalloporphyrin	Equivalents Li	
	Ætioporphyrin I (% yield) ^a	<i>meso</i> -Tetraphenylporphin (% yield) ^a
Sn ^{IV}	750 (92)	—
Fe ^{III} ^b	750	—
Cu ^{II}	1000	250
Co ^{II}	1500	700
Co ^{III}	1500	—
Ni ^{II}	2000	750 (99 ^d ; 69 ^e)
VO ^{II}	2750	—
Pd ^{II}	3000 (65 ^e)	2000
Pt ^{II}	No reaction	3000 ^e (18)

^a Determined spectroscopically. ^b Iron octaethylporphin. ^c Yield by isolation of porphyrin.
^d 73% Reduction. ^e Side reactions.

requirement and ranges from 250 equivalents † in the case of copper *meso*-tetraphenylporphin to 3000 in the case of platinum *meso*-tetraphenylporphin. When smaller amounts of lithium are used the reactions do not go to completion even after prolonged boiling. They do not appear to be time-dependent and proceed either rapidly or not at all. This also applies to reactions with lithium solution and other lithium derivatives (see below).

Correlation of the stability of a metalloporphyrin with the amount of lithium required gives the order Pt > Pd > VO > Ni > Co^{II} > Cu > Sn^{IV}, Fe^{III}, in agreement with the results obtained by other workers using different methods (see above).

The reactions generally proceeded cleanly in high yield (see Table 1) except in the case of platinum *meso*-tetraphenylporphin, where side reactions occurred with the formation of unidentified by-products. The fact that cobaltic ætioporphyrin I bromide required the same amount of lithium (1500 equivalents) as the cobaltous complex is explained by the (observed) reduction of the former to the latter before demetallation. This casts doubt on the correct position of Sn^{IV} and Fe^{III} in the above series. By analogy with Co^{III} it can be postulated that the amounts of lithium required for the demetallation of iron and tin porphyrins relate to the Sn^{II} and Fe^{II} complexes. Hence results must be interpreted with caution when dealing with metalloporphyrins in which the metal is not in a bivalent state.

Platinum ætioporphyrin I was the only metalloporphyrin which resisted demetallation even with a very large excess of lithium (20,000 equivalents). It also resisted demetallation with hot concentrated sulphuric acid, as did palladium ætioporphyrin I, and palladium and platinum *meso*-tetraphenylporphin. Palladium octaethylchlorin (VI) was converted into palladium octaethylporphin under these conditions.

In most cases some reduction of the porphyrin ring occurred, particularly when very large excesses of lithium were used. The reduction products were colourless, presumably of the porphyrinogen type, similar to the products obtained by chemical (metal-acid)²⁵ or

* The primary reaction of a metalloporphyrin with lithium-ethylenediamine is of course the formation of the dilithio-complex but since this is converted into the metal-free porphyrin by water the reaction is referred to as "demetallation" for convenience.

† One equivalent of lithium = 2 atoms per porphyrin molecule.

²⁵ E.g., Fischer and Rothhaas, *Annalen*, 1930, **484**, 85; Mauzerall and Granick, *J. Biol. Chem.*, 1958, **232**, 1141, and references cited therein.

photochemical²⁶ reduction or by catalytic hydrogenation.²⁷ They could be quantitatively reoxidised to the porphyrin by high-potential quinones.²⁸ This reaction is in striking contrast to the sodium-alcohol reduction of iron octaethylporphyrin which afforded di-, tetra-, and hexa-hydroporphyrins.²⁰ No intermediates of this type were encountered in the present work.

We next attempted demetallation by using lithium which had been dissolved in ethylenediamine before addition of the metalloporphyrin. The blue colour, produced when lithium is dissolved in ethylenediamine, which is believed to be due to solvated free electrons,²⁹ is rapidly discharged at the boiling point. Demetallation, however, proceeds smoothly even with lithium solutions which have been boiled for two hours. The amount of lithium required is essentially the same as in the case of reactions with solid metal (see Table 2) and the initial reflux period has only a slight effect (see Experimental section).

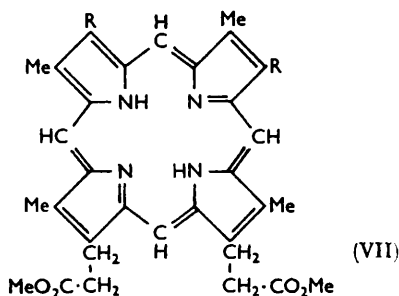
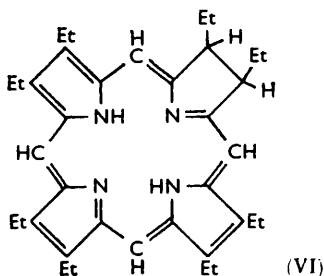
TABLE 2.
Demetallation with solutions of lithium in ethylene diamine.

Metalloporphyrin	Equivalents Li	
	Ætioporphyrin I (% yield) ^a	<i>meso</i> -Tetraphenylporphyrin (% yield) ^a
Cu ^{II}	1000 (105 ^b)	500 (90 ^b)
Co ^{II}	1500	1000 ^c (20)
Co ^{III}	1500	—
Ni ^{II}	2000 (91)	1000
Pd ^{II}	> 3000	2000 ^c (0)
Pt ^{II}	—	3000 ^c (0)

^a Determined spectroscopically. ^b 21—23% Reduction. ^c Side reactions.

Side reactions were more pronounced in the case of the *meso*-tetraphenylporphyrin derivatives, in particular for the cobaltous complex which gave a low porphyrin recovery (20%) and the palladium and platinum derivatives which yielded only products of unknown structure which were not further investigated.

One of the principal advantages of the lithium solution is the fact that reduction is greatly minimised. Thus, for example, 500 equivalents of solid lithium completely reduce copper *meso*-tetraphenylporphyrin whereas, with the same amount of dissolved lithium, reduction occurs to only 23%. The usefulness of the lithium solution is particularly



apparent in the case of porphyrins with reducible substituents. This is shown most strikingly in the case of copper 2,4-diacetyldeuteroporphyrin dimethyl ester (VII; R = Ac). With solid lithium this is reduced to the corresponding copper hæmatoporphyrin (VII; R = CHMe·OH) * which is then demetallated with approximately 1000 equivalents

* Evidence for the formation of (VII; R = CHMe·OH) is based on spectral data and is supported by the fact that lithium-ethylenediamine reduces carbonyl compounds to alcohols.²¹

²⁶ Mauzerall, *J. Amer. Chem. Soc.*, 1962, **84**, 2437.

²⁷ Fischer and Bub, *Annalen*, 1937, **530**, 213.

²⁸ Eisner and Linstead, *J.*, 1955, 3749.

²⁹ Windwer and Sundheim, *J. Phys. Chem.*, 1962, **66**, 1254.

of lithium whereas with lithium solution (500 equivalents) smooth conversion into dilithiodiacetyldeuteroporphyrin dimethyl ester takes place. Isolation of metal-free diacetyldeuteroporphyrin dimethyl ester (VII; R = Ac) proved difficult owing to its solubility properties, and further work was precluded by lack of material. Attempted demetallation of *meso*-tetra-4-pyridylporphin (III; R = C₅H₄N) complexes with solid lithium resulted in decomposition, whereas lithium solution afforded the metal-free porphyrin (III; R = C₅H₄N).

The effects of concentration and temperature have not been investigated systematically. In general, the amount of lithium required for complete demetallation increases with decreasing reaction temperature and metalloporphyrin concentration. Thus, for example, copper *meso*-tetraphenylporphin was demetallated by 500 equivalents of lithium (solution) at 115° whilst 1000 equivalents were required at room temperature. When the concentration of copper *meso*-tetraphenylporphin was halved, 1500 equivalents of lithium were needed for complete demetallation at room temperature.

Application of our method to a comparison of the stabilities of metalloporphyrins containing the same metal but different ligands results in a stability order ætioporphyrin I > *meso*-tetraphenylporphin > *meso*-tetra-4-pyridylporphin > diacetyl-

TABLE 3.

Metalloporphyrin	Equivalents Li ^a	Reflux Period ^b	% Yield ^c
Cu Ætio ^d	1000	1 min.	105
Cu TPP ^e	500	1 min.	90
Cu TPP ^e	1000	30 min.	—
Cu TpyP ^f	1000	30 min.	74
Co TPP ^e	1000	2 min.	20
Co TpyP ^f	1000	2 min.	52
Pd OEC ^g	2000	—	70
Pd Ætio ^d	3000	—	—

^a All experiments with lithium solution except the last two in which solid was used. ^b Of lithium solution prior to addition of porphyrin. ^c Determined spectroscopically. ^d Ætio = ætioporphyrin I. ^e TPP = *meso*-tetraphenylporphin. ^f TpyP = *meso*-tetra-4-pyridylporphin. ^g OEC = octaethylchlorin.

deuteroporphyrin dimethyl ester, which is that expected from the relative positions of the spectral bands of the corresponding metal complexes.

This order is probably also related to the decreasing base strengths ^{1,30} of the metal-free porphyrins and clearly demonstrates weakening of the metal–nitrogen bonds by electron-withdrawing substituents in the periphery of the porphyrin molecule. The fact that the copper and cobaltous complexes of (III; R = Ph) and (III; R = C₅H₄N) have approximately the same stability is not surprising since it has been shown ^{14,31} that differently substituted aromatic groups in the *meso*-position exert only a slight effect on the electronic transitions of the porphyrin ring system, and hence on the metal–nitrogen bond strength. The observed stability order is the reverse of that encountered in acid demetallations where it has been found ¹⁰ that complexes of the less basic porphyrins are more difficult to demetallate. We have confirmed this by the qualitative data shown in Table 4.

These observations can be readily explained by the initial attack of one or more protons on the metalloporphyrin nitrogens ^{5,15} to give a protonated intermediate. The complexes derived from less basic porphyrins will thus be demetallated less readily, although their metal–nitrogen bonds are weaker. On the other hand, acid demetallation of a series of metalloporphyrins in which different metals are chelated to the same ligand will be facilitated by the increasing polarity of the metal–nitrogen bond ^{5,15} and the ease of demetallation will increase with decreasing thermodynamic stability of the complex.

³⁰ Fleischer and Webb, *J. Phys. Chem.*, 1963, **67**, 1131.

³¹ Thomas and Martell, *J. Amer. Chem. Soc.*, 1956, **78**, 1338.

TABLE 4.

Metalloporphyrin	N-H ₂ SO ₄ in CH ₃ ·CO ₂ H	2N-H ₂ SO ₄ in CH ₃ ·CO ₂ H
Cu \AA tio ^c	Demetallated ^a	Demetallated ^a
Cu TPP ^d	Unchanged ^b	Demetallated ^a
Cu diAc ^e	Unchanged ^b	Partially demetallated ^b
Ni \AA tio ^c	Slightly demetallated ^b	Partially demetallated ^b
Ni TPP ^d	Insoluble	Insoluble
Ni diAc ^e	Unchanged ^b	Unchanged ^b

^a Instantly on warming. ^b After boiling for 3 min. ^c \AA tio = \AA tioporphyrin I. ^d TPP = *meso*-tetraphenylporphin. ^e diAc = diacetyldeuteroporphyrin dimethyl ester.

The lithium-ethylenediamine demetallations, unlike reactions in acid media, can therefore give a direct indication of the metal-nitrogen bond strength in a metalloporphyrin.

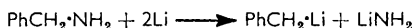
Metallochlorins appear to be demetallated more readily than the corresponding porphyrins both in acid¹⁰ and in basic media although they are known¹ to be less basic. Presumably in the less aromatic chlorin system other factors determine the ease of breaking the metal-nitrogen bonds.

We next attempted to elucidate the mechanism of the demetallation reaction. It was readily shown that demetallation was not due to an exchange reaction of the type



where MP is a metalloporphyrin, since prolonged boiling of a solution of copper *meso*-tetraphenylporphin with a very large excess of anhydrous lithium acetate did not result in replacement of copper by lithium. It could similarly be shown that the anion (H₂N·CH₂·CH₂·NH)⁻, produced by reaction of ethylenediamine with phenyl-lithium, was inactive. Prolonged boiling of a solution of copper or cobalt *meso*-tetraphenylporphin in ethylenediamine with phenyl-lithium did not affect the metalloporphyrin. It has been reported³² that lithium bromide, present in phenyl-lithium prepared in the usual manner from bromobenzene and lithium, inhibits certain reactions. Accordingly phenyl-lithium was prepared from diphenylmercury³³ but even in this case no reaction took place with copper or cobalt *meso*-tetraphenylporphin or copper diacetyldeuteroporphyrin dimethyl ester.

Krabbe³⁴ showed that the following reaction takes place when benzylamine is treated with lithium in ether:



A solution of lithium amide in boiling ethylenediamine demetallated copper *meso*-tetraphenylporphin as effectively as lithium-ethylenediamine. Lithium hydride could be used instead of lithium amide.

No reaction took place when lithium hydride and copper *meso*-tetraphenylporphin were boiled in dibutyl ether but addition of ethylenediamine caused rapid demetallation. Lithium hydride was also used to demetallate nickel \AA tioporphyrin I and copper *meso*-tetraphenylporphin. Nickel *meso*-tetra-4-pyridylporphin, however, resisted demetallation under conditions whereby nickel \AA tioporphyrin I was demetallated. Nickel and cobaltous diacetyldeuteroporphyrin dimethyl ester appeared to be demetallated but isolation of the metal-free porphyrin was again not possible.

Other primary amines in the presence of lithium, lithium hydride, or amide were also able to demetallate copper *meso*-tetraphenylporphin (Table 5).

The results are not strictly comparable with the ethylenediamine system because of the different reaction temperatures and of the lower solubilities of the lithium salts in the systems tried. This probably explains why larger excesses and longer reflux periods are needed in some cases. Pyridine, the only tertiary amine tried, and lithium amide (1000 equivalents) had no effect on copper *meso*-tetraphenylporphin.

³² Huisgen and Mack, *Chem. Ber.*, 1960, **93**, 332.

³³ Huisgen, Mack, and Moebius, *Tetrahedron*, 1960, **9**, 29.

³⁴ Krabbe and Grunwald, *Ber.*, 1941, **74**, 1343.

TABLE 5.

Amine	Reagent	Equiv.	Reflux Period (hr.)	Temp.	Reaction* (% yield)
BuNH ₂	LiH or LiNH ₂	1000	9	77°	No reaction
BuNH ₂	Li	2000	{ 8 60	77 20	99
C ₆ H ₁₁ ·NH ₂	LiNH ₂	1000	2	131	Complete
C ₆ H ₁₁ ·NH ₂	Li	2000	{ 3 15	131 20	Complete
PhCH ₂ ·NH ₂	LiNH ₂	1000	0.25	184	Complete

* Undissolved reagent was present at the end of every reaction.

One of the products isolated from the reaction of ethylenediamine with lithium in the presence of certain hydrocarbons is the bi-imidazoline (VIII).³⁵ We were able to isolate it in low yield from ethylenediamine and lithium hydride. This compound or a related



substance such as (IX; R = H) was thought to be the reactive species for two reasons: either it might function as a very powerful chelating agent and successfully compete with the porphyrin for the metal, or else it might be a free-radical precursor, as has been shown with (IX; R = Ph).³⁶ Pure bi-imidazoline (VIII) and lithium hydride in boiling dibutyl ether did not affect copper *meso*-tetraphenylporphyrin. On the other hand, when (VIII) was prepared *in situ* from ethylenediamine and thio-oxamide³⁷ in the presence of copper *meso*-tetraphenylporphyrin the latter was smoothly demetallated after prolonged boiling. This represents the first demetallation under basic conditions *without the intervention of another metal ion*. Thiourea, in very large excess, produced essentially the same result although the product was not entirely pure. Oxamide proved ineffective. Thio-oxamide is known to have a very strong affinity for copper but it was readily shown that it did not act as a competing chelating agent since demetallation did not take place on boiling it with copper *meso*-tetraphenylporphyrin in dibutyl ether or cyclohexylamine. Another powerful chelating agent, acetylacetone, did not demetallate copper *meso*-tetraphenylporphyrin in the presence of lithium hydride, even after addition of pyridine.

A free-radical mechanism for the demetallation reaction appeared to be an attractive hypothesis. One-electron reduction of the central metal atom to a lower valency state would greatly diminish the stability of the complex and displacement by lithium ions to give the more stable dilithio-complex would then be feasible. Preparation of copper^I and copper⁰ phthalocyanine complexes by reaction of copper phthalocyanine with potassium in ammonia has been described,³⁸ as has the reduction of zinc *meso*-tetraphenylporphyrin to the zinc^I and zinc⁰ complexes with sodium anthracene or sodium ketyls,³⁹ and of manganese phthalocyanine to the Mn^I and Mn⁰ derivatives with lithium-benzophenone.⁴⁰ The reagents in all these cases are known to contain free radicals. We tried, unsuccessfully, to demetallate copper *meso*-tetraphenylporphyrin in dibutyl ether or ethylenediamine with tetraphenylhydrazine or diphenylpicrylhydrazyl. However, biphenyl-lithium in tetrahydrofuran⁴¹ was a very effective demetallating agent for copper *meso*-tetraphenylporphyrin, reaction taking place at room temperature with 250 equivalents of lithium. In the course of some work on the negative phthalocyanine ion

³⁵ Reggel, Henry, and Wender, *J. Org. Chem.*, 1961, **26**, 1837.

³⁶ Lemal and Kawano, *J. Amer. Chem. Soc.*, 1962, **84**, 1761.

³⁷ Lehr and Erlenmeyer, *Helv. Chim. Acta*, 1944, **27**, 489.

³⁸ Watt and Dawes, *J. Inorg. Nuclear Chem.*, 1960, **14**, 32.

³⁹ Closs and Closs, *J. Amer. Chem. Soc.*, 1963, **85**, 818.

⁴⁰ Taube and Munke, *Angew. Chem.*, 1963, **75**, 639.

⁴¹ Eisch and Kaska, *Chem. and Ind.*, 1961, 470.

produced from magnesium phthalocyanine and sodium anthracene, Terenin *et al.*⁴² noted some absorption bands which they assigned to sodium phthalocyanine without commenting on the implications of this observation.

Examination of some of our reagents and reaction mixtures by electron spin resonance (e.s.r.) and absorption spectroscopy was inconclusive. Lithium hydride or amide in ethylenediamine gave e.s.r. signals which differed with different preparations of the sample. Thio-oxamide in ethylenediamine alone or in the presence of copper *meso*-tetraphenylporphyrin did not give a signal. Copper *meso*-tetraphenylporphyrin in lithium-ethylenediamine solution gave a signal which disappeared on admission of air. The same solution showed several absorption bands in the near infrared region (cf. ref. 39) which also disappeared in the presence of air. Copper *meso*-tetraphenylporphyrin in the presence of thio-oxamide and ethylenediamine did not absorb in this region.

We next attempted to inhibit the reaction by means of various inhibitors. Addition of tetraphenylhydrazine to a solution of lithium hydride in ethylenediamine immediately discharged the blue colour of the solution but on addition of copper *meso*-tetraphenylporphyrin demetallation took place in the usual way. A large amount of quinol appeared to react with lithium hydride in ethylenediamine but the resulting mixture was still able to cause partial demetallation of copper *meso*-tetraphenylporphyrin. A similar result was obtained with the thio-oxamide-ethylenediamine system in the presence of quinol. Finally it was found that demetallation of copper *meso*-tetraphenylporphyrin with lithium hydride in ethylenediamine proceeded normally in a current of dry air.

These reactions indicate that free radicals, although present in some of the systems, are not directly involved in the demetallation. The reagents which successfully demetallate metalloporphyrins (lithium or its derivatives in ethylenediamine and other amines, thioamides in ethylenediamine, biphenyl-lithium) are so diverse that it is difficult to conceive of a common factor which may be operative, unless it be reduction of the central metal atom to a lower valency state. Even this hypothesis seems untenable in view of the fact that reaction proceeds in the presence of air, and the question must therefore be left open at present. It is of course possible that different mechanistic pathways are operative for the various reagents, especially the thioamide systems.

EXPERIMENTAL

Spectroscopic measurements were carried out on a Hartridge reversion spectroscope (qualitative) and on a Unicam S.P. 500 spectrophotometer (quantitative).

Materials.—Ætioporphyrin I,⁴³ octaethylporphyrin,¹⁹ octaethylchlorin,²⁰ a-tetrahydro-octaethylporphyrin²⁰ and *meso*-tetraphenylporphyrin⁴⁴ were prepared by standard methods and were purified by adsorption chromatography on alumina or magnesia and crystallisation, as were the copper, cobaltous, and nickel derivatives of ætioporphyrin I²³ and *meso*-tetraphenylporphyrin.¹⁴

We gratefully acknowledge gifts of *meso*-tetra-4-pyridylporphyrin⁴⁵ and its complexes from Dr. J. N. Phillips, Division of Plant Industry, C.S.I.R.O., Canberra, of 2,4-diacetyldeuteroporphyrin dimethyl ester and its derivatives from Dr. W. S. Caughey, Johns Hopkins Medical School, Baltimore; of cobaltic ætioporphyrin I bromide⁴⁶ from Professor A. W. Johnson, The University, Nottingham; of vanadyl ætioporphyrin I from Mr. R. A. Dean, B.P. Research Centre, Sunbury-on-Thames; and of bisbenzonnitrilepalladous chloride from Dr. D. B. Powell, Sir John Cass College, London.

Stannic Ætioporphyrin I Dichloride.—This was prepared by the method of Corwin and Collins.²² It was obtained as a dark red powder, insoluble in the common organic solvents, and was used without further purification [Found: C, 56.6; H, 5.2; Cl, 12.0. C₃₂H₃₆Cl₂N₄Sn requires C, 57.7; H, 5.4; Cl, 10.7%].

⁴² Shablya and Terenin, *Optics and Spectroscopy*, 1960, **9**, 280.

⁴³ McEwen, *J. Amer. Chem. Soc.*, 1946, **68**, 712; Treibs and Schmidt, *Annalen*, 1952, **577**, 111.

⁴⁴ Aronoff and Calvin, *J. Org. Chem.*, 1943, **8**, 205.

⁴⁵ Fleischer, *Inorg. Chem.*, 1962, **1**, 493.

⁴⁶ Johnson and Kay, *J.*, 1960, 2979.

Palladium Ætioporphyrin I.—Ætioporphyrin I (39 mg.) and bisbenzotrilepalladous chloride ⁴⁷ (71 mg.) were heated in boiling benzene for 1 hr. The solution was concentrated under reduced pressure and chromatographed on alumina (grade I). Ether eluted palladium ætioporphyrin I (39 mg., 82%) which crystallised from chloroform-methanol in red needles.

Platinum Ætioporphyrin I.—Ætioporphyrin I (32.4 mg.) and bisbenzotrile platinumous chloride ⁴⁷ (76 mg.) in benzonitrile (40 ml.) were heated to boiling for 3 hr. The solvent was removed under reduced pressure and the residue chromatographed on alumina (grade I). Elution with benzene-ether (1 : 1) followed by two crystallisations from chloroform-methanol afforded red microcrystals of *platinum ætioporphyrin I* (38.0 mg., 84%); λ_{max} (in benzene) 382, 503, 537 m μ (ϵ 232,000; 11,700; 53,600) [Found: C, 57.0; H, 5.25; N, 8.2. C₃₂H₃₂N₄Pt requires C, 57.2; H, 5.4; N, 8.3%].

Palladium Octaethylchlorin.—Octaethylchlorin (120 mg., 1 mol.) and bisbenzotrilepalladous chloride (18.6 mg., 1.3 mol.) in benzene (20 ml.) were boiled under reflux in an atmosphere of nitrogen for 30 min. A further portion of bisbenzotrilepalladous chloride (23 mg.) was added, boiling was continued for 1 hr. and the solution was kept overnight under nitrogen. Chromatography on magnesia (grade II) gave the following fractions: (a) benzene eluted a faint green band (λ_{max} 603, 626 m μ) followed by the main fraction of palladium octaethylchlorin; (b) ether eluted traces of octaethylchlorin and palladium octaethylporphin. *Palladium octaethylchlorin* crystallised from benzene-methanol in purple needles (9.5 mg., 40%); λ_{max} (in benzene) 396, 483, 518, 559, 602 m μ (ϵ 87,200; 4800; 5800; 8100; 64,900) [Found: C, 67.1; H, 7.3; Pd, 16.7. C₃₆H₄₆N₄Pd requires C, 67.4; H, 7.2; Pd, 16.7%].

Solutions of platinum octaethylchlorin (λ_{max} 596 m μ) and platinum a-tetrahydro-octaethylporphin (λ_{max} 494, 632 m μ) were prepared from the metal-free pigments and bisbenzotrileplatinous chloride in warm benzonitrile; palladium a-tetrahydro-octaethylporphin (λ_{max} 498, 631 m μ) was similarly prepared from the corresponding palladium complex in benzene at room temperature.

Palladium meso-Tetraphenylporphin.—*meso*-Tetraphenylporphin (15.4 mg., 1 mol.) and palladous chloride (5.8 mg., 1.3 mol.) in benzonitrile (20 ml.) were heated to boiling for 5 min. The solution was cooled to 100° and hot methanol (50 ml.) was added. The product (14.8 mg.) was collected after 2 days and chromatographed on alumina (grade I). Elution with benzene and crystallisation from chloroform-methanol afforded pure palladium *meso*-tetraphenylporphin (8.6 mg., 48%).

Platinum meso-Tetraphenylporphin.—*meso*-Tetraphenylporphin (17.6 mg.) and bisbenzotrileplatinous chloride (15.6 mg.) in benzonitrile (20 ml.) were boiled under reflux for 1 hr. The solution was evaporated to dryness under reduced pressure and the residue chromatographed on alumina (grade I). Elution with benzene-light petroleum (1 : 1) followed by crystallisation from chloroform-methanol afforded pure platinum *meso*-tetraphenylporphin (9 mg., 39%).

Demetallation Reactions.—Unless otherwise stated all reactions were carried out in an atmosphere of pure dry nitrogen.

Purification of materials. Ethylenediamine monohydrate was boiled under reflux with potassium hydroxide pellets for 2 days and then with sodium for 2 days. The anhydrous material was twice distilled from sodium and stored in a microburette fitted with a soda-lime tube.

Nitrogen. White-spot nitrogen was bubbled successively through alkaline pyrogallol solution, concentrated sulphuric acid, potassium hydroxide pellets, and anhydrous magnesium perchlorate.

Lithium wire (25.4 mg./cm.) was extruded from a 0.1 in. die and stored under sodium-dried benzene.

General procedure for demetallations with solid lithium. The metalloporphyrin was weighed into a 50-ml. round-bottomed flask fitted with a nitrogen inlet and a condenser with a tapered outlet and ethylenediamine was added to produce an approximately 10⁻⁴M-solution. Nitrogen was passed and solution was ensured by boiling for 30–60 min. Lithium wire of known length was added through the condenser and boiling was continued, samples being withdrawn through the condenser at intervals.

Samples were examined for the presence of the metal-free porphyrin by hand spectroscope (a)

⁴⁷ Kharasch, Seyler, and Mayo, *J. Amer. Chem. Soc.*, 1938, **60**, 882.

directly for the presence of the dilithio-complex and (b) after dilution with benzene or chloroform, followed by washing with water and drying. The solution prepared under (b) was sometimes treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in order to detect reduced porphyrins, or with concentrated hydrochloric acid to convert any metal-free porphyrin to its dication. For spectroscopic determination of porphyrin content a known volume of reaction solution was treated as under (b), the resulting benzene solution made up to a known volume and examined in a Unicam S.P. 500 spectrophotometer. In some cases the spectral measurement was repeated after addition of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in order to determine percentage reduction.

The following experiment is typical for demetallation of *ætioporphyrin I* and *meso*-tetraphenylporphin derivatives.

Nickel *meso*-tetraphenylporphin (1.94 mg.) in ethylenediamine (20 ml.) was treated with lithium (3×0.4 cm., 750 equivalents) during 1 hr., reaction then being complete. Spectroscopic analysis gave a porphyrin recovery of 99% and a reduction level of 73%.

Preparative demetallation of palladium ætioporphyrin I. Palladium *ætioporphyrin I* (25.0 mg.) in ethylenediamine (50 ml.) was treated with lithium (59.0 cm.; 2500 equiv.) during 4 hr. The cooled solution was diluted with benzene, water was cautiously added, and the aqueous layer neutralised with hydrochloric acid and repeatedly extracted with chloroform. The combined extracts were washed with water and evaporated to dryness under reduced pressure. The residue was crystallised from chloroform-methanol and chromatographed on alumina (grade I). Elution with benzene-ether (1:1) and crystallisation from chloroform-methanol afforded pure *ætioporphyrin I* (13.2 mg., 65%).

Copper-2,4-diacetyldeuteroporphyrin dimethyl ester (1.06 mg.) in ethylenediamine (10 ml.) was treated with lithium (0.2 cm., 250 equivalents). After 30 min. a sample showed the spectrum of copper hæmatoporphyrin dimethyl ester (λ_{max} 532, 566 m μ). Addition of more lithium (3×0.2 cm.) over 1 hr. resulted in almost complete replacement of copper by lithium.

Cobalt diacetyldeuteroporphyrin dimethyl ester and cobalt and nickel *meso*-tetra-4-pyridylporphin, on treatment with lithium (500, 500, and 1000 equivalents, respectively) under these conditions, were completely decomposed.

General procedure for demetallation with a solution of lithium in ethylenediamine. Lithium wire was dissolved in ethylenediamine in an atmosphere of nitrogen and boiled for a specified period. A solution of the metalloporphyrin in ethylenediamine was added and sampling was carried out as before.

The following experiment is typical for demetallation of *ætioporphyrin I* and *meso*-tetraphenylporphin derivatives.

Lithium (0.8 cm., 500 equiv.) in ethylenediamine (10 ml.) was boiled until the colour had been discharged when copper *meso*-tetraphenylporphin (2.03 mg.) in ethylenediamine (10 ml.) was added. Reaction was complete after 30 min. Spectroscopic determination gave a reduction level of 23% and a porphyrin recovery of 90%.

Similar experiments, in which the initial reflux period before the addition of copper *meso*-tetraphenylporphin, the concentration, and the amount of lithium used were varied, are tabulated below.

Lithium equiv.	Initial reflux period (min.)	Copper TPP • concn. (mg/20 ml.)	TPP • recovered (%)
500	5	1	No reaction
500	2	2	90
1000	5	1	71
1000	10	1	89
1000	120	2	98

• TPP = *meso*-tetraphenylporphin.

Reaction at room temperature. Lithium (3.2 cm., 2000 equiv.) was added to ethylenediamine (10 ml.) and the solution was stirred magnetically until the colour had disappeared (1.5 hr.). Copper *meso*-tetraphenylporphin (2.02 mg.) in ethylenediamine (10 ml.) was added and reaction was complete after 15 min.

A number of similar experiments, in which the amount of lithium and the copper *meso*-tetraphenylporphin concentration were varied, are tabulated below.

Lithium equiv.	Copper TPP concn. (mg./20 ml.)	Result
750	2	No reaction
1000	1	No reaction
1000	2	Complete reaction
1500	1	Complete reaction

Copper 2,4-diacetyldeuteroporphyrin dimethyl ester. Lithium (0.35 cm., 500 equiv.) in ethylenediamine (9 ml.) was boiled for 30 min., and copper diacetyldeuteroporphyrin dimethyl ester (0.90 mg.) in ethylenediamine (11 ml.) was added. After 15 min. the solution showed the spectrum of dilithiodiacetyldeuteroporphyrin dimethyl ester (λ_{max} , 581, 624 m μ). Decomposition with water and extraction into benzene failed owing to solubility factors. However, neutralisation of the mixture with hydrochloric acid and dilution with acetone gave a faint spectrum of the metal-free porphyrin.

Cobaltous and nickel 2,4-diacetyldeuteroporphyrin dimethyl ester, under similar conditions on treatment with lithium (1000 equiv.) appeared to be at least partially demetallated.

Copper meso-tetra-4-pyridylporphin. Lithium (1.8 cm., 1000 equiv.) in ethylenediamine (10 ml.) was boiled for 30 min., and a solution of copper meso-tetra-4-pyridylporphin (2.25 mg.) in ethylenediamine (10 ml.) was added. Reaction was essentially complete after 15 min. The product was a mixture of starting material (12%) and metal-free porphyrin (74%).

Cobaltous meso-tetra-4-pyridylporphin and lithium (1000 equiv.) under the same conditions gave the metal-free porphyrin in 52% yield, but the corresponding nickel complex was unaffected by boiling with lithium (1500 equiv.) for 5 hr.

Reactions with Lithium Hydride.—(a) *Copper meso-tetraphenylporphin.* Lithium hydride (12.0 mg., 500 equiv.) in ethylenediamine (5 ml.) was boiled for 1.5 hr. A solution of copper meso-tetraphenylporphin (1.0 mg.) in ethylenediamine (5 ml.) was added. Reaction was complete after 15 min. with a porphyrin recovery of 92%. An analogous result was obtained with 250 equivalents of lithium hydride.

(b) *Nickel α tioporphyrin I.* Lithium hydride (59.0 mg., 2000 equiv.) and nickel α tioporphyrin I (0.94 mg.) in ethylenediamine (10 ml.) were boiled for 4 hr., partial replacement of the nickel occurring. Reaction was complete after boiling for a further 3 hr. No reaction was observed with 1000 equivalents of lithium hydride.

(c) *Copper meso-tetra-4-pyridylporphin.* Lithium hydride (5.9 mg., 250 equiv.) in ethylenediamine (5 ml.) was boiled for 1.5 hr. and copper meso-tetra-4-pyridylporphin (1.00 mg.) in ethylenediamine (5 ml.) was added. Reaction was complete after 5 min. with a porphyrin recovery of 43%.

(d) *Nickel meso-tetra-4-pyridylporphin* was unaffected after 5 hours' treatment with lithium hydride (2000 equiv.) as in the preceding experiment.

(e) *Cobaltous and nickel 2,4-diacetyldeuteroporphyrin dimethyl ester.* With lithium hydride (1000 and 1500 equiv., respectively) under the same conditions, these appeared to be demetallated although it was not possible to isolate the product.

Reactions with Lithium Amide.—(a) *Copper meso-tetraphenylporphin.* Lithium amide (30.3 mg., 250 equiv.) in ethylenediamine (10 ml.) was boiled for 15 min., and copper meso-tetraphenylporphin (1.80 mg.) in ethylenediamine (10 ml.) was added. Reaction was complete after 15 min. with a porphyrin recovery of 91%. A similar experiment with 125 equivalents of lithium amide gave a porphyrin recovery of 9%.

(b) *Nickel 2,4-diacetyldeuteroporphyrin dimethyl ester.* With lithium amide (1500 equiv.) this appeared to be demetallated after 4 hr., but the product could not be isolated.

Reactions in Other Amines.—The amines were purified by being refluxed over potassium hydroxide followed by fractional distillation.

(a) Copper meso-tetraphenylporphin (0.98 mg.) in *n*-butylamine (10 ml.) was treated with lithium (0.4 cm., 500 equiv.), and the solution was boiled for 3 hr. Very little of the lithium had reacted and no change was observed. More lithium (1.2 cm., 1500 equiv.) was added and boiling was continued for 5 hr.; the copper had then been partially replaced by lithium. The solution was kept at room temperature for 2 days and reaction was found to be complete with a porphyrin recovery of 99%.

(b) With lithium amide or lithium hydride (1000 equiv.) and copper meso-tetraphenylporphin in *n*-butylamine no change was observed after boiling for 9 hr.

(c) Lithium amide (71.4 mg., 1000 equiv.) and copper *meso*-tetraphenylporphin (1.06 mg.) in cyclohexylamine (10 ml.) were boiled for 2 hr. Reaction was then complete although much lithium amide remained undissolved.

(d) Copper *meso*-tetraphenylporphin (1.05 mg.) in cyclohexylamine (10 ml.) was treated with lithium (0.4 cm., 500 equiv.), and the solution was boiled for 3 hr. The lithium had not completely dissolved but some reaction had taken place. More lithium (1.2 cm., 1500 equiv.) was added and the solution was boiled for 3 hr. and kept at room temperature for 15 hr.; reaction was then complete. Undissolved lithium was still present.

(e) Lithium amide (76.0 mg., 1000 equiv.) was dissolved in boiling benzylamine (5 ml.) and copper *meso*-tetraphenylporphin (1.14 mg.) in benzylamine (5 ml.) was added. Reaction was essentially complete after boiling for 15 min.

Bis- Δ^2 -2-imidazolynyl.—Lithium hydride (2.0 g.) in ethylenediamine (30 ml.) was boiled for 3 hr. and more ethylenediamine (5 ml.) was added to the viscous solution. Boiling was continued for 7.5 hr. and the cooled mixture was then poured into water (300 ml.). The product (0.39 g.) was filtered off, washed with water and acetone, and dried. Sublimation at 180°/1 mm. afforded bis- Δ^2 -2-imidazolynyl as needles, m. p. (sealed tube) 290—295° (decomp.), [lit.,^{46,37} m. p. 289—291° (decomp.); 290—298°] [Found: C, 52.1; H, 7.3. Calc. for C₈H₁₀N₄: C, 52.2; H, 7.25%]. It was characterised as the picrate, m. p. 275—277° (lit.,^{46,37} m. p. 272—273°; 284—285°).

Reaction with Thio-oxamide.—Thio-oxamide (88.5 mg., 500 mol.) in ethylenediamine (10 ml.) formed a dark green thermochromic solution. Copper *meso*-tetraphenylporphin (0.86 mg., 1 mol.) was added and the solution was boiled for 13.5 hr.; reaction was then essentially complete, with a porphyrin recovery of 84%.

In similar experiments with di-*n*-butyl ether or cyclohexylamine instead of ethylenediamine no reaction was observed.

Reaction with Thiourea.—Copper *meso*-tetraphenylporphin (0.92 mg., 1 mol.) and thiourea (154 mg., 1500 mol.) in ethylenediamine (10 ml.) were boiled for 5 hr. No change was observed. A large excess of thiourea was added and boiling was continued for a further 4 hr.; all the starting material had then disappeared. The product consisted essentially of *meso*-tetraphenylporphin but was contaminated with another material, λ_{max} , 649 m μ .

Reaction with Biphenyl-lithium.—Biphenyl (86.0 mg.) in freshly distilled tetrahydrofuran⁴⁹ (5 ml.) was treated with lithium (0.25 cm., 250 equiv.), and the solution stirred magnetically at room temperature for 2 hr. Copper *meso*-tetraphenylporphin (1.20 mg.) in tetrahydrofuran (5 ml.) was added and reaction was complete after 1 min. Prolonged contact with the reagent destroyed the pigment.

When lithium was added to a solution of biphenyl and copper *meso*-tetraphenylporphin in tetrahydrofuran in an analogous experiment a mixture was produced consisting of *meso*-tetraphenylporphin and a material of λ_{max} , 635 m μ .

Attempted Inhibition of the Reaction.—(a) *With tetraphenylhydrazine.* Lithium hydride (5.7 mg., 250 equiv.) in ethylenediamine (5 ml.) was boiled for 2 hr. giving a deep blue solution. Addition of tetraphenylhydrazine⁵⁰ (48.6 mg., 100 mol.) immediately discharged the colour giving a reddish-brown solution. Copper *meso*-tetraphenylporphin (0.97 mg., 1 mol.) in ethylenediamine (5 ml.) was added and demetallation was complete after 5 min.

(b) *With quinol.* (i) Lithium hydride (5.9 mg., 250 equiv.) in ethylenediamine (5 ml.) was boiled for 2 hr. Addition of quinol (33.6 mg., 250 mol.) immediately discharged the colour and precipitated a white material. Copper *meso*-tetraphenylporphin (0.97 mg., 1 mol.) in ethylenediamine (5 ml.) was added and the solution was boiled for 4 hr.; partial replacement of the copper took place. (ii) Copper *meso*-tetraphenylporphin (1.10 mg.) and thio-oxamide (98 mg., 500 equiv.) in ethylenediamine (10 ml.) were treated with excess of quinol (115 mg.). The reaction was partially complete after 6 hr.

(c) *With air.* Lithium hydride (5.7 mg., 250 equiv.) in ethylenediamine (5 ml.) was boiled in a current of dry air (soda-lime) for 2 hr. To the resulting pale orange solution copper *meso*-tetraphenylporphin (0.97 mg.) in ethylenediamine (5 ml.) was added. Reaction was complete after 5 min.

Election Spin Resonance Measurements.—These were carried out on a Hilger Microspin

⁴⁶ Woodburn and O'Gee, *J. Org. Chem.*, 1952, **17**, 1235.

⁴⁹ Paul, Lipkin, and Weissmann, *J. Amer. Chem. Soc.*, 1956, **78**, 116.

⁵⁰ Wieland and Gambarjan, *Ber.*, 1906, **39**, 1499.

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E.S.R.1 spectrometer. We are indebted to Mr. H. M. Assenheim, of Hilger and Watts Ltd., for the measurements and for helpful discussions.

(a) Lithium hydride and lithium amide, severally, in ethylenediamine were sealed into silica tubes, using vacuum line techniques. Heating for 5 min. produced a dark brown solution in each case which gave essentially identical spectra consisting of 5 groups of 5 lines having an intensity ratio 1 : 4 : 6 : 4 : 1 and a g value ~ 2 .

(b) Lithium amide was dissolved in boiling ethylenediamine and the dark blue solution was transferred to a silica tube under nitrogen and sealed. A single peak, g 2.0001, line width ~ 0.5 gauss, was obtained.

(c) A partially demetallated solution of copper *meso*-tetraphenylporphin (1 mg./20 ml.) with lithium (1500 equiv.) in ethylenediamine showed a single peak with a g value ~ 2 , which disappeared in the presence of air.

This solution had $\lambda_{\text{max.}}$, 737, 842, 965 μ . In the presence of air these bands were replaced by the dilithio-*meso*-tetraphenylporphin spectrum.

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