

Concerning *meso*-Tetraphenylporphyrin Purification¹

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Treatment of crude *meso*-tetraphenylporphyrin with 2,3-dichloro-5,6-dicyanobenzoquinone affords a high recovery of 'chlorin-free' *meso*-tetraphenylporphyrin (1), the excess of quinone and its transformation products being easily removed by adsorption on alumina. This new procedure is also applied to the purification of *meso*-tetraphenylporphyrin metal complexes.

meso-TETRAPHENYLPORPHYRIN (TPP) (1) has been extensively employed for investigation of the physical and spectroscopic properties of the porphyrin macrocycle and its diverse metal complexes.² This fact can be related directly to the ease with which TPP can be pre-

¹ Preliminary communication, G. H. Barnett, M. F. Hudson, and K. M. Smith, *Tetrahedron Letters*, 1973, 2887.

² E.g. 'The Chemical and Physical Behavior of Porphyrin Compounds and Related Structures,' ed. A. D. Adler, *Ann. New York Acad. Sci.*, 1973, vol. 206, and references therein.

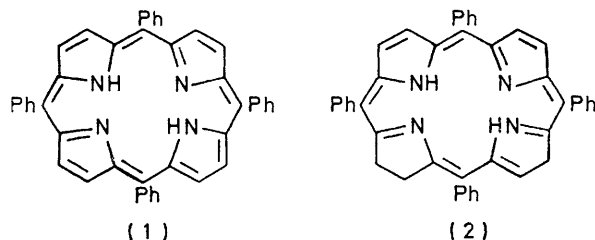
pared on a large scale by following the general approach developed by Rothmund,³ and optimised by Adler and his co-workers,⁴ such that brief refluxing of equimolar proportions of pyrrole and benzaldehyde in propionic acid furnishes a 20% yield of crude TPP from the cooled

³ P. Rothmund and A. R. Menotti, *J. Amer. Chem. Soc.*, 1941, **63**, 267.

⁴ A. D. Adler, F. R. Longo, J. D. Finarelli, J. Goldmacher, J. Assour, and L. Korsakoff, *J. Org. Chem.*, 1967, **32**, 476.

solution.* However, the TPP is invariably contaminated with 2–10% of *meso*-tetraphenylchlorin (TPC) (2) which is difficult to remove.

Earlier workers employed a variety of methods for removal of the admixed TPC, typical examples being (i) repeated filtration through a bed of Fuller's earth⁴ (which also disposes of 80% of the material), (ii) sublimation⁴ with variable success⁵ (and no recovery reported), (iii) chromatography, either of the zinc complex in trichloroethylene on talc,⁵ or on Florisil⁶ (with no convincing evidence for product purity), (iv) heating for several hours in dimethyl sulphoxide⁷ (no recovery reported), and (v) photo-oxidation of the zinc complex in benzene.^{5,8}



Since the conversion of chlorins into porphyrins by oxidation with high-potential quinones is firmly established⁹ we considered the possibility of transformation of chlorin into porphyrin rather than separation of the two when developing a new method for purification of TPP. TPC in crude TPP is not oxidised by chloranil,⁵ but we found that treatment of the crude TPP-TPC mixture with an excess of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in boiling methylene chloride or chloroform rapidly and conveniently accomplishes the transformation of the TPC into TPP. Work-up requires removal of the excess of quinone and its products, and we have optimised this (*cf.* ref. 1) such that it merely involves filtration of the hot reaction mixture under suction through a bed of Brockmann grade I alumina in a sintered glass funnel. In this way, 20 g of TPP-TPC mixture can be processed by using only 300 g of alumina; concentration of the filtrate and dilution with methanol results in crystallisation of 19.2 g (96%) of chlorin-free TPP.†

Purity of TPP is best judged by measurement of the visible absorption spectrum, usually in benzene. The contaminant causes enhanced absorption at *ca.* 650 nm due to superposition of the TPC long-wavelength band (654 nm) upon band I (647 nm) of the TPP spectrum. The percentage contamination with TPC is easily calculated⁵ and all samples prepared by the DDQ

* We have found that a second crop of TPP can be obtained by concentration of the mother liquors.

† The overall recovery depends largely upon the purity of the starting material; however, the material prepared by the Adler procedure⁴ is usually of very high quality.

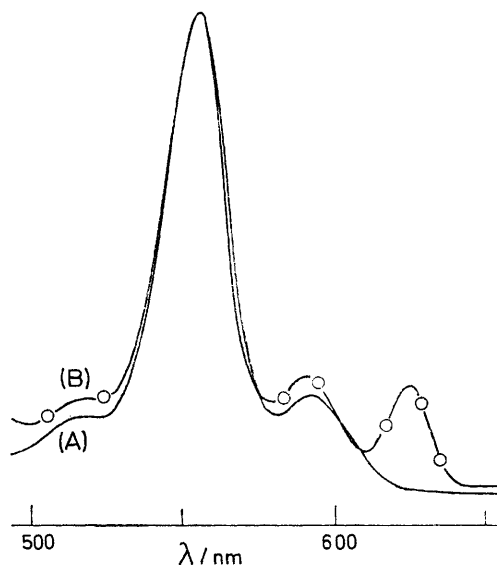
⁵ G. M. Badger, R. Alan Jones, and R. L. Laslett, *Austral. J. Chem.*, 1964, **17**, 1028.

⁶ W. Bhatti, M. Bhatti, P. Imbler, A. Lee, and B. Lorenzen, *J. Pharm. Sci.*, 1972, **61**, 307.

method were chlorin-free by this criterion. Mass spectrometry is not an acceptable technique for estimation of TPC owing to the ready electron-impact-induced dehydrogenation of the chlorin.¹⁰

It is not convenient to estimate the degree of TPC contamination of a sample while the DDQ reaction is in progress, mainly because one usually requires accurate molar extinction coefficients in benzene solution. However, chlorin-free metal complexes of TPP are often required and since most metallo-TPP complexes possess virtually no absorption around 625 nm, it is a simple matter to carry out the DDQ reaction on metal complexes (without an accessible higher oxidation state) and monitor the diminution of the long-wavelength metallo-chlorin band (Figure). In this way, chlorin-free zinc(II) TPP and copper(II) TPP were obtained from the crude complexes with recoveries of 87 and 91%, respectively. Complexation with, for example, zinc(II) also provides a rapid method for the qualitative identification of chlorin in a sample.

Our procedure, as described in the preliminary communication,¹ has been criticised¹¹ as 'unnecessary, and on a large scale both irksome and expensive.' These workers prefer¹¹ dry column chromatography on the



Visible absorption spectra in chloroform of (A) chlorin-free zinc(II) TPP; (B) contaminated zinc(II) TPP (Soret band omitted)

0.5 g scale (200 g alumina), though they acknowledge this to be expensive. On the large scale (1 g and greater) the Canadian group¹¹ preferred our DDQ procedure but

⁷ N. Datta-Gupta and G. E. Williams, *J. Org. Chem.*, 1971, **36**, 2019.

⁸ G. D. Dorrough and F. M. Huennekens, *J. Amer. Chem. Soc.*, 1952, **74**, 3974.

⁹ *E.g.* U. Eisner and R. P. Linstead, *J. Chem. Soc.*, 1955, 3749; U. Eisner, A. Lichtarowicz, and R. P. Linstead, *ibid.*, 1957, 733.

¹⁰ M. Meot-Ner, A. D. Adler, and J. H. Green, *Org. Mass Spectrometry*, 1973, **7**, 1395.

¹¹ K. Rousseau and D. Dolphin, *Tetrahedron Letters*, 1974, 4251.

with the alumina work-up¹ replaced by lengthy solvent extraction involving extraction with 1% sodium hydroxide solution containing sodium dithionite, three further washings with water, drying over sodium sulphate, filtration, and then evaporation and crystallisation in the usual way.

The developments reported herein, in which 20 g of crude TPP can be efficiently processed by using only 300 g of alumina, more closely represent the potential of the DDQ procedure as outlined in our preliminary publication. We suppose that volumes of solvents required to apply the solvent extraction modification¹¹ to 20 g of TPP would be prohibitive.

EXPERIMENTAL

meso-Tetraphenylporphyrin.—Benzaldehyde (66.5 ml) and pyrrole (46.5 ml) were added simultaneously to refluxing propionic acid (2.5 l) and the mixture was refluxed for a further 30 min before being set aside overnight at room temperature. The product was filtered off, then washed with hot water and then methanol (filtrate collected separately from propionic acid) until the filtrate was colourless, and gave purple glistening crystals (20.4 g, 19.8%). The visible absorption spectrum in benzene indicated⁵ ca. 5% contamination with TPC (Found: C, 85.1; H, 4.9; N, 9.2. Calc. for $C_{44}H_{30}N_4$: C, 86.0; H, 4.9; N, 9.1%, indicating the crude material to be of a similar composition to that prepared by Adler⁴). Concentration of the propionic acid mother liquors to ca. 500 ml afforded a second crop of TPP (6.0 g; total yield 26%). The recovered propionic acid was refluxed for 3 h with potassium dichromate (30 g) and then distilled before re-use.

'Chlorin-free' *meso-Tetraphenylporphyrin* (1).—Crude TPP (20 g) was dissolved in refluxing ethanol-free chloroform (2.5 l) before addition of DDQ (5 g) in dry benzene

(150 ml). The mixture was refluxed during 3 h before filtration of the yellowish solution under suction through a sintered glass funnel (2.5 in diam. \times 8 in) containing alumina (300 g; Fluka, Brockmann grade I).^{*} The alumina was washed with methylene chloride (200 ml) and the combined filtrates were concentrated to ca. 200 ml before addition of methanol (200 ml). Filtration afforded the product (19.2 g, 96%) as glistening purple crystals. The visible absorption spectrum in benzene [λ_{max} 482 (ϵ 3 400), 515 (18 900), 548 (8 000), 592 (5 300), and 648 nm (3 400)] showed no contamination with TPC.⁵ In a smaller scale reaction [TPP (1 g), methylene chloride (250 ml), DDQ (250 mg) in benzene (15 ml)] only 30 min heating under reflux was required. After purification by use of alumina,¹ the product (940 mg, 94%) was similarly shown to be chlorin-free by spectrophotometry (Found: C, 86.1; H, 5.1; N, 9.0. Calc. for $C_{44}H_{30}N_4$: C, 86.0; H, 4.9; N, 9.1%).

Zinc(II) meso-Tetraphenylporphyrin.—Crude zinc(II) TPP [λ_{max} 422 (ϵ 390 000), 514 (3 800), 548 (19 500), 587 (4 500), and 613 nm (6 800)] (1 g) [obtained by treatment of crude TPP in methylene chloride with a saturated solution of zinc(II) acetate in methanol, followed by the usual work-up] was refluxed in methylene chloride (220 ml) for 15 min before addition of DDQ (250 mg) in benzene (15 ml). The mixture was heated under reflux for 1 h before filtration under suction through a sintered glass funnel (1 in diam. \times 6 in) containing alumina (15 g; Fluka, Brockmann grade I). The filtrate was concentrated to ca. 20 ml and diluted with methanol (20 ml). The product was filtered off, washed with methanol, then dried to give a purple crystalline solid (879 mg, 88%), λ_{max} 422 (ϵ 574 000), 512 (3 300), 548 (24 000), and 589 nm (4 200).

Similarly, a 91% yield of copper(II) TPP was obtained from the crude metal complex.

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* A filter paper was placed on top of the alumina to prevent disturbance of the bed during pouring.