meso-Thiocyanatoporphyrins as Intermediates in the Synthesis of Sulphur Analogues of the Oxophlorins

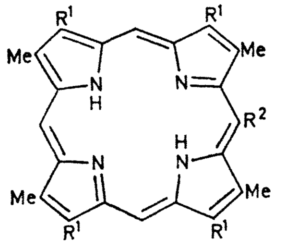
By P. S. CLEZY* and C. J. R. FOOKES

(*Department of Organic Chemistry, The University of New South Wales, P.O. Box 1, Kensington, N.S.W., 2033, Australia*)

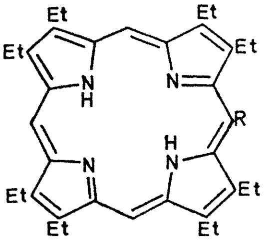
Summary The copper complexes of porphyrins react with thiocyanogen at room temperature to give *meso*-thiocyanato-derivatives which upon hydrolysis with 90% sulphuric acid yield sulphur analogues of the oxophlorins.

ALTHOUGH thiocyanation of pyrroles has been reported by a number of workers[1] this reaction seems not to have been investigated with the tetrapyrrolic porphyrin macrocycle. We undertook a study of this substitution reaction as it appeared to offer a possible synthesis of the *meso*-sulphur porphyrins analogous to the oxophlorins. We reported earlier[2] the first preparation of this class of compound and discussed the unusual n.m.r. spectrum of this species in neutral solvent.

When a chloroform solution of the copper complex of *coproporphyrin* II diethyl ester (1 mmole) was allowed to react at room temperature with thiocyanogen† (3 mmoles) in acetic acid the *meso*-thiocyanato-derivative was obtained. This compound was treated briefly (2 min) in the cold with concentrated sulphuric acid to give the metal-free tetrapyrrole which was purified by preparative t.l.c. on silica. We formulate this product as (**1a**),‡ [m.p. 253°; $\lambda_{\max}$ $CHCl_3$ (log ϵ): 633 (3·83), 581 (3·70), 548 (3·95), 512 (3·94), 409 (5·07), and 395 infl (4·95) nm; τ (CF_3CO_2D): $-0·94$ (2H), $-0·64$ (1H) (methines), 5·70 (q, 2 × OCH_2CH_3), 5·80 (q, 2 × OCH_2CH_3), 5·8 (m, 4 × CH_2CH_2CO), 6·36 (2 × CH_3), 6·42 (2 × CH_3), 6·88 (m, 2 × CH_2CH_2CO), 6·95 (m, 2 × CH_2CH_2CO), 8·68 (t, 2 × OCH_2CH_3), and 8·78 (t, 2 × OCH_2CH_3)]. On stereochemical grounds it would be expected that substitution between the methyl groups would be preferred and this structure is confirmed by n.m.r. spectroscopy. In trifluoroacetic acid the methine protons of coproporphyrin II appear as a doublet (2: 2) and Abraham *et al.*[3] have assigned the resonance at lower field to the protons situated between the propionic ester residues. In the thiocyanato-derivative the low-field resonance still contains two protons while the signal at higher field corresponds to a single proton. This is in agreement with structure (**1a**) for this derivative.



(1) a; $R^1 = [CH_2]_2 \cdot CO_2Et$; $R^2 = SCN$
b; $R^1 = [CH_2]_2 \cdot CO_2Me$; $R^2 = SH$



(2) a; R = SCN
b; R = SH

Hydrolysis of (**1a**) with 90% (w/w) sulphuric acid for 20 min on a steam bath followed by esterification with methanolic acid and purification by preparative t.l.c. gave the *meso*-mercapto-derivative (**1b**), [m.p. 234—235°; $\lambda_{\max}$ $CHCl_3$ (log ϵ): 655 (3·71), 650 infl (3·68), 592 (3·95), 510 infl (4·00), and 396 (4·90) nm; τ ($CDCl_3$): $-0·08$ (1H), 1·55 (2H) (methines), 5·80 (m, 2 × CH_2CH_2CO), 6·29 (2 × CH_3), 6·41 (2 × OCH_3), 6·62 (2 × OCH_3), 7·02 (m, 2 × CH_2CH_2-CO), 7·68 (2 × CH_3), 8·10 (m, 2 × CH_2CH_2CO), 8·25 (m, 2 × CH_2CH_2CO), and 13·25 (1H), 14·40 (1H) (NH)]. This compound can be obtained directly from the copper complex (**1a**) by hydrolysis with 90% sulphuric acid; this is an easier preparative procedure since the purification of (**1a**) is a tedious operation.

The spectroscopic data derived from (**1b**) closely resembled that reported[2] for the original example of this class of tetrapyrrole. In particular, while the n.m.r. spectrum of (**1b**) in CF_3CO_2D was consistent with its formulation as the dication of (**1b**), in $CDCl_3$ the protons associated with two methine carbons, a pair of methyls and a pair of propionic ester residues were located at much higher field than were normally found for a typical porphyrin. The high-field position of two pairs of methyl groups was observed in the n.m.r. spectrum ($CDCl_3$) of the previously reported[2] member of this class and it was this feature which led us to suggest that the neutral molecule was a rapidly equilibrating mixture of tautomers.

Thiocyanation of octaethylporphin has also been achieved to give (**2a**) although a higher concentration of thiocyanogen (10 mmoles) is required in this case. Hydrolysis of (**2a**) gives (**2b**).

Unlike most porphyrins compounds (**1b**) and (**2b**) showed only small molecular ions (*ca.* 5%) in their mass spectra; the base peak in both cases was at $M - 32$. Thionaphthols have been reported[4] to lose sulphur in the mass spectrometer.

The preparation of *meso*-sulphur porphyrins by this route has improved the accessibility of this class of compound as yields by this method are greatly in excess of those obtained by the original thione procedure.[2]

We acknowledge financial support from the Australian Research Grants Committee.

(*Received, July 20th, 1971; Com.* 1253.)

---

† Thiocyanogen was prepared by the dropwise addition of bromine to ammonium thiocyanate dissolved in the minimum volume of acetic acid.

‡ Satisfactory analytical data were obtained for all compounds.

[1] P. Pratesi, *Atti Accad. naz. Lincei*, **1932**, **16**, 443 [*Chem. Abs.*, 1933, **27**, 2442]; D. S. Matteson and H. R. Snyder, *J. Org. Chem.*, 1957, **22**, 1500; S. Gronowitz, A.-B. Hörnfeldt, B. Gestblom, and R. A. Hoffman, *ibid.*, 1961, **26**, 2615; E. Söderback, S. Gronowitz, and A.-B. Hörnfeldt, *Acta Chem. Scand.*, 1961, **15**, 227; R. K. Olsen and H. R. Snyder, *J. Org. Chem.*, 1963, **28**, 3050.

[2] P. S. Clezy and G. A. Smythe, *Chem. Comm.*, 1968, 127.

[3] R. J. Abraham, A. H. Jackson, and G. W. Kenner, *J. Chem. Soc.*, 1961, 3468.

[4] S.-O. Lawesson J. Madsen, G. Schroll, J. H. Bowie, and D. H. Williams, *Acta Chem. Scand.*, 1966, **20**, 2325.