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OXOPHLORIN (OXYPORPHYRIN) SYNTHESIS

S.W. McCombie and K.M. Smith*

Robert Robinson Laboratories, University of Liverpool,

P.O. Box 147, Liverpool, L69 3BX

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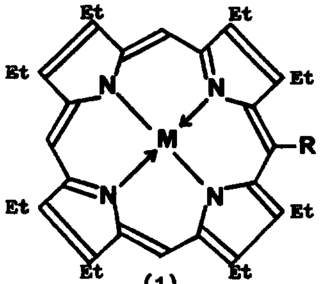
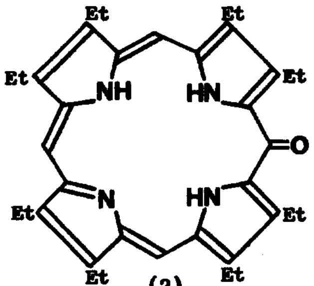
Recent radiochemical labelling experiments have led to the conclusion[1] that oxophlorin iron complexes are intermediates in the catabolism of the haemoproteins to bile pigments.[2] This result had been anticipated for some time and consequently a great deal of work on the synthesis of oxophlorins (e.g. 2) has been carried forward.[3]



(1)



(2)

a) M = Fe.py$_2$; R = H b) M = Fe; R = OCOPh

c) M = Mg; R = H d) M = Zn; R = H

Ring synthesis is the only acceptable route to biologically significant oxophlorins, but large quantities of oxophlorins for model studies can be prepared, usually in moderate yield, by treatment of porphyrins with benzoyl peroxide (followed by de-benzoylation),[4] or else by oxidation of iron porphyrins with reaction mixtures containing hydrogen peroxide (followed by de-metallation).[5] The best method[6] of this type is the oxidation of the pyridine haemochrome (1a) with hydrogen peroxide in pyridine, followed by treatment with benzoyl chloride, de-metallation of (1b) and then hydrolysis to octaethyloxophlorin (2) in an overall yield of 36% from the haem (1a).

We have recently found[7] that treatment of porphyrins with an excess of thallium(III) trifluoroacetate gives thallium(III) porphyrin chelates which are inert to further attack by the excess oxidising agent. However, we now report that treatment of

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* Address correspondence to this author.

the magnesium or zinc porphyrins (**1c,d**) with thallium trifluoroacetate gives high yields of the oxophlorin (**2**). Typically, zinc octaethylporphyrin (**1d**; 415 mg.) in dry THF (30 ml.) and dichloromethane (100 ml.) was treated with a solution of thallium trifluoroacetate (480 mg.; 1.25 equiv.) in THF (20 ml.) and the mixture stirred at room temperature for one minute. Water (0.25 ml.) in THF (10 ml.) was then added (solution turned from purple to red) and the solution was stirred for a further 10 minutes. After brief treatment with sulphur dioxide (Tl(III) salts → Tl(I) salts) the mixture was stirred for 5 minutes with conc. hydrochloric acid (2 ml.) and then the products were extracted into chloroform which was dried (Na_2SO_4) and evaporated to dryness. Chromatography on Brockmann Grade III alumina in dichloromethane gave octaethyloxophlorin (**2**; 302 mg.; 79%) after crystallisation from dichloromethane / methanol. [M.p. 254 - 256° (Lit.[6] 255°). *Found*: C, 78.54; H, 8.30; N, 10.23%. *Calc. for* $C_{36}H_{46}N_4O$, C, 78.50; H, 8.42; N, 10.17%.]

The reaction reported herein is analogous to the recently reported[8] formation of phenols from benzenoid compounds, and may therefore involve aromatic electrophilic thallation. Experiments to determine the origin of the oxophlorin oxygen atom and also the range of metalloporphyrins to which this reaction can be applied will be reported in a full paper.

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