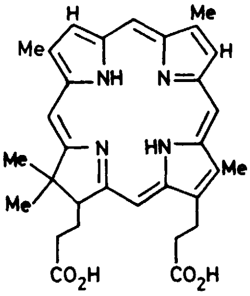
Synthesis of the Chlorin Macrocycle by a Photochemical Approach

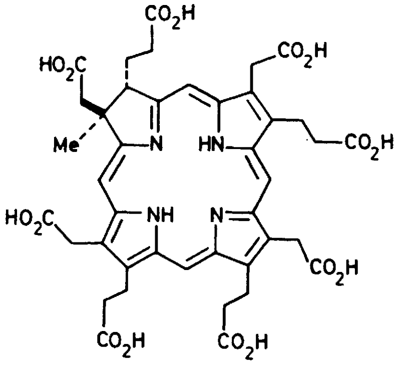
Alan R. Battersby,* Christopher J. Dutton, Christopher J. R. Fookes, and Simon P. D. Turner
University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, U.K.

A practical synthesis of the chlorin macrocycle has been developed which depends on a mild photochemical cyclisation as the key step.

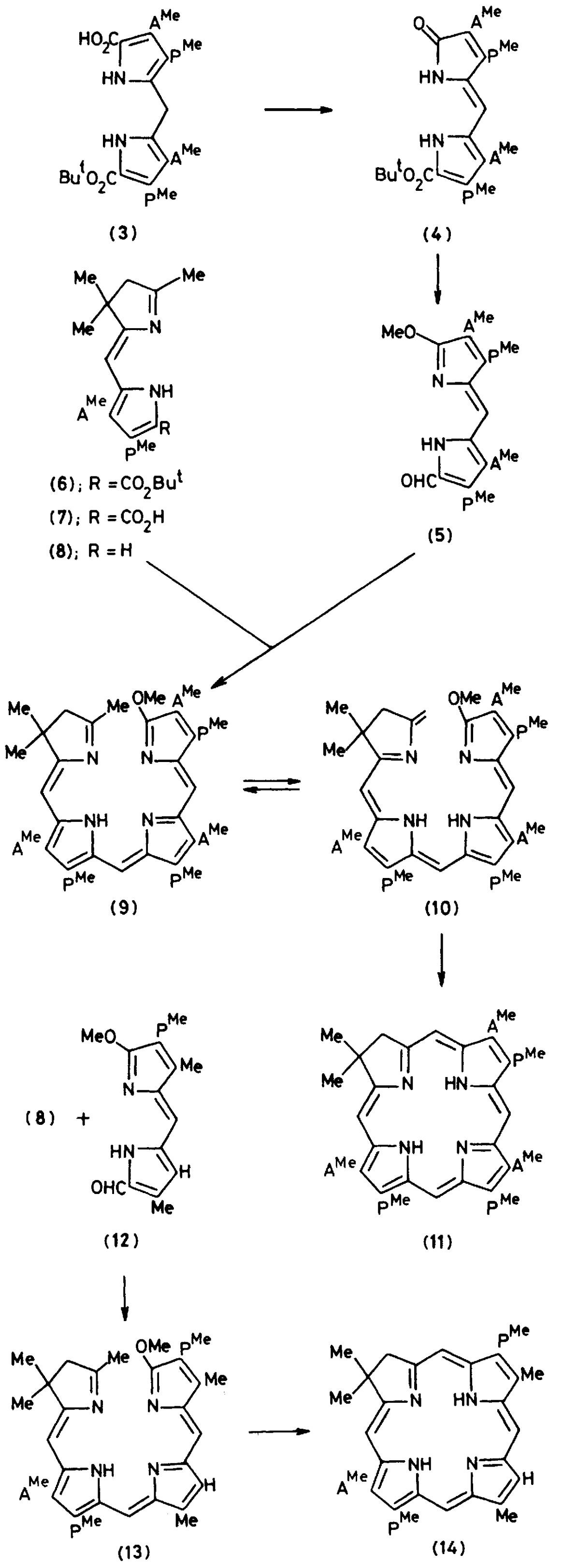
The chemistry of natural chlorins (*e.g.* the chlorophylls) has recently been enriched by the discovery of *C*-methylated chlorins, the most important being bonellin[1] (**1**) and Faktor I[2] (**2**); the latter is of significance in relation to vitamin B_{12}.



(1)



(2)



$A^{Me} = CH_2CO_2Me$

$P^{Me} = CH_2CH_2CO_2Me$

Synthetic routes to simpler model chlorins have been described[3,4] which in principle could be used for building the natural products (**1**) and (**2**). However, the more recent development of a photochemical route to isobacteriochlorins[5] led us to explore the possibility that chlorins might also be accessible by photochemical ring-closure of a suitable seco-precursor. The successful development of such a route is now outlined.

The pyrromethane[6] (**3**) was converted by mild oxidative bromination and hydrolysis[7] retaining the t-butyl ester, into the pyrromethenone (**4**), 51%. The t-butyloxycarbonyl group was then replaced by a formyl group, 87% yield, using trifluoroacetic acid (TFA) followed by trimethyl orthoformate. *O*-Methylation of the product with trimethyloxonium tetrafluoroborate produced one component (**5**) for the seco-system in 59% yield. The other component (**6**) had been synthesised earlier.[5] Acid-catalysed condensation of (**5**) with the pyrrole (**8**), generated by TFA from (**6**) *in situ*, *via* (**7**), yielded the seco-system (**9**), which in tetrahydrofuran containing TFA and Hünig's base was irradiated with light from tungsten lamps. This yielded the crystalline chlorin (**11**), m.p. 172—173 °C, in 54% overall yield for the four steps from the precursors (**5**) and (**6**), representing an average yield for each step of greater than 85%. A reasonable mechanism for the conversion of (**9**) into (**11**) involves photochemical ring-closure of the 18π-tautomer (**10**) followed by loss of methanol. Attention is drawn to the close similarity of this chlorin (**11**) to Faktor I (**2**).

In a similar way, the imino ether aldehyde (**12**) (the synthesis of which is outlined in the following communication[8]), was condensed with the same western half (**8**) to generate the seco-system (**13**). Irradiation as before then gave the chlorin (**14**) in 26% overall yield from the dipyrrolic units (**8**) and (**12**). Note the resemblance of (**14**) to bonellin (**1**).

The chlorins (**11**) and (**14**) were chosen as targets because they exemplify all the reactive functions of the natural products (**1**) and (**2**), *e.g.* acetate and propionate side-chains, unsubstituted positions on the macrocycle. These functions are handled very satisfactorily by the photochemical approach, its mildness being a major advantage.

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