Site-specific Reduction of Unsymmetrically Substituted Porphyrins to give Isomerically Pure Chlorins†

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Photoreduction, in the presence of ascorbic acid and diazabicyclo[2.2.2]octane, of zinc(II) vinylporphyrins, affords vinylchlorins in which the macrocyclic double bond in the pyrrole subunit bearing the vinyl group is regioselectively *cis*-reduced; when a vinylporphyrin bearing a more strongly electron-withdrawing methoxycarbonyl group is photoreduced, the ester-bearing ring is regioselectively reduced.

Hydroporphyrins have become increasingly important because of their involvement in a variety of biological systems.[1] We recently showed[2] that the Seely photoreduction[3] of magnesium(II) and zinc(II) vinylchlorins [in pyridine–ethanol with ascorbic acid and diazabicyclo[2.2.2]octane (DABCO)] gives initially a vinyl isobacteriochlorin, which subsequently rearranges to an ethylidene isobacteriochlorin with the 'isobacteriochlorophyll-b' chromophore. The dependence of the regioselectivity of this photoreduction upon the presence of an electronegative substituent (the vinyl) led us to speculate that this same reduction could be used to carry out site-specific reductions of unsymmetrically substituted *porphyrins* to give isomerically pure chlorins. Current methods for chlorin formation from porphyrins, with one exception,[4] are non-selective with regard to the ring being reduced,[5] and are subject to over-reduction and poor yields. A photoreduction of pheoporphyrins to *cis*-pheophorbides has previously been reported by Wolf and Scheer,[6] but the driving force for the ring D selectivity was presumably more steric than electronic. In the present paper we show that photoreduction of zinc(II) porphyrins can be electronically controlled to give isomerically pure chlorins.

Irradiation of zinc(II) 4-methyl-4-devinylprotoporphyrin-IX dimethyl ester (**1**)[7] under fluorescent lamps in the presence of DABCO and ascorbic acid gave a sharp band at 466 nm (Krasnovskii intermediate[8]?) which reached maximum intensity after one hour. This band gradually disappeared and a band at 618 nm grew in intensity such that after 20 hours of irradiation the 618 nm band was the strongest long wavelength

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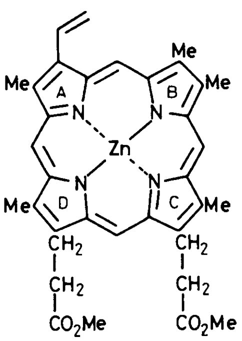
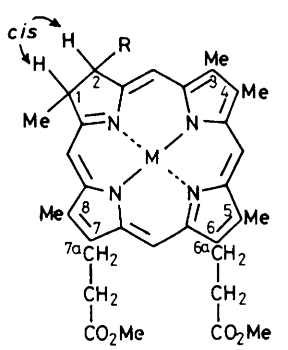
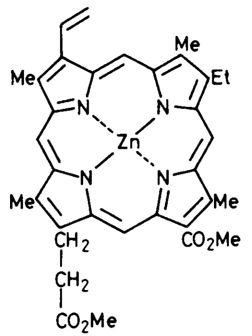
† In this communication the Fischer system of numbering the porphyrin derivatives is used rather than the I.U.P.A.C.–I.U.B. recommended system. The relationship between the two systems for positions relevant to this communication is as follows (I.U.P.A.C.–I.U.B. numbering in parentheses: 1(2), 2(3), 3(7), 4(8), 5(12), 6(13), 7(17), 8(18), 6a(13^1), 7a(17^1), 2a(3^1), and 2b(3^2).



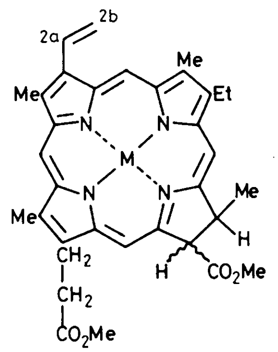
(1)



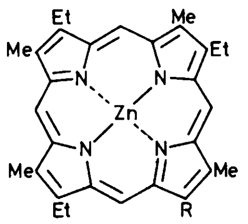
(2) M = Zn; R = CH=CH2
(3) M = Zn; R = Et
(4) M = 2H; R = Et



(5)



(6) M = Zn
(7) M = 2H



(8) R = CH=CHCO2Me
(9) R = CH2CH2CO2Me
(10) R = CH=CHCO2H

absorption in the visible spectrum.‡ To avoid isomerization to ethylidenechlorin[2] and to ethylporphyrin, the product zinc(II) 2-vinyl-4-methylchlorin (2) was not isolated but was catalytically reduced (over palladized charcoal) to give zinc(II) 2-ethylchlorin (3); there was no evidence of reduction of any macrocyclic unsaturation in this step. Demetallation with trifluoroacetic acid gave the free base (4) which was purified and characterized. The ^{1}H n.m.r. spectrum showed the high and low field *meso*-protons (δ 9.70, 9.69, 8.86, and 8.85) expected of a chlorin. Two triplets (δ 4.33 and 4.20) were assigned to the 6a- and 7a-CH_2, indicating either ring A or B as the site of reduction. One methyl doublet (δ 1.93, J 7.2 Hz) and a high field methyl triplet (δ 1.09, J 7.2 Hz) as well as the absence of a low field methylene confirmed that ring A was the sole site of reduction. Decoupling experiments allowed assignment of a doublet of quartets (δ 4.63) to 1-H and a multiplet at δ 4.45 to 2-H. When the latter multiplet was decoupled, 1-H collapsed to a quartet and revealed J 2.5 Hz coupling for the 1- and 2-H. From the coupling constant (2.5 Hz) of the 1- and 2-H protons it may be inferred that the ring is reduced to give predominantly the *cis*-relative configuration.

Photoreduction of zinc(II) 2-vinylrhodoporphyrin-XV dimethyl ester (5), which contains two electron-withdrawing groups but on rings opposite each other, led only to the ring C-reduced chlorin (6) with no over-reduction apparent. It was evident from the visible absorption spectrum of the reaction mixture that reduction did not occur in either ring B or D. The n.m.r. spectrum of the reduced zinc complex clearly indicated that ring A had not been reduced since the vinyl protons (2a-H, δ 8.2—8.1; 2b,2b′-H, δ 6.2—5.85) were only slightly shifted (δ 0.2) from those of the corresponding porphyrin (5). Two distinct sets of signals were observed for several protons indicating that the product existed as a mixture of *cis*- and *trans*-isomers. ^{1}H N.m.r. decoupling experiments at 5-H (m, δ 5.11) showed that two different signals for 6-H (d, δ 5.72, J 10.0 Hz and d, δ 5.24, J 4.1 Hz) collapsed, confirming that (6) [and by analogy, (7)] was a mixture of *cis*- and *trans*-isomers. The zinc(II) complex was then demetallated to give the free base (7), and this step caused production of some porphyrin, suggesting that chlorin had oxidized during demetallation. The *trans*- to *cis*-isomer ratio was greater in (7) than in (6), indicating that the thermodynamically less favoured *cis*-isomers were oxidized preferentially. With the acidic nature of the 6-H it seems logical that the kinetic reduction products are also the *cis*-isomers which under the basic reaction conditions equilibrate to the more thermodynamically favourable *trans*-products.

Attention then turned to photoreduction of a porphyrin acrylate (**8**). The photoreduction/vinyl migration process (even with benzene as the solvent) was very facile for the acrylate system; several attempts to isolate a chlorin from the photoreduction failed. Although a chlorin could be observed spectrophotometrically in the early stages of the photoreduction the only product that could be isolated was the acrylate-reduced (*i.e.* propionate) porphyrin (**9**). Conversion into this porphyrin was very rapid, was independent of the amount of DABCO present, and occurred with both the acrylic methyl ester (**8**) and the acrylic acid (**10**).

The photoreduction is ring-specific, depending upon the substituents present; this has obvious value in regiospecific formation of hydro-porphyrins from porphyrins. Further investigations are underway to determine the range of electronegative substituents which are effective directors, and to develop a procedure for synthesis of complex chlorins.

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‡ All reactions described in this paper proceeded in good yield, as determined by spectrophotometry, but owing to lability (during handling and chromatography) of the *cis*-reduced products towards oxidation and rearrangement, no attempts have so far been made to optimize yields. New compounds were characterized by ^{1}H n.m.r. spectroscopy, spectrophotometry, elemental analysis, and/or high resolution mass spectrometry.