3,8-Diethynyl-3,8-devinylprotoporphyrin IX Dimethyl Ester and its Haemin

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Treatment of 3,8-diacetyldeuteroporphyrin IX dimethyl ester **6** with phosphoryl chloride and *N,N*-dimethylformamide gives the 3,8-bis(1-chloro-2-formylvinyl) derivative **7** which affords the corresponding 3,8-diethynyl derivative **2** upon treatment with base; compound **2** and its iron(III) chloride dimethyl ester are fully characterized.

Protohaem, the iron(II) complex of protoporphyrin IX **1**, is the prosthetic group in a large number of haemoglobins, myoglobins, cytochromes, catalases and peroxidases.[1] In many haem proteins, the haem 3- and 8-vinyl groups (IUPAC nomenclature) play an important role in modulating haem reactivity through protein–haem interactions.[2] A wide variety of derivatives of **1** have been synthesized in which the 3- and 8-vinyl groups have been replaced together or individually with hydrogen, formyl, methyl, ethyl, acetyl, (1-hydroxyethyl), (2-hydroxyethyl), halogens, nitriles and other functionali-

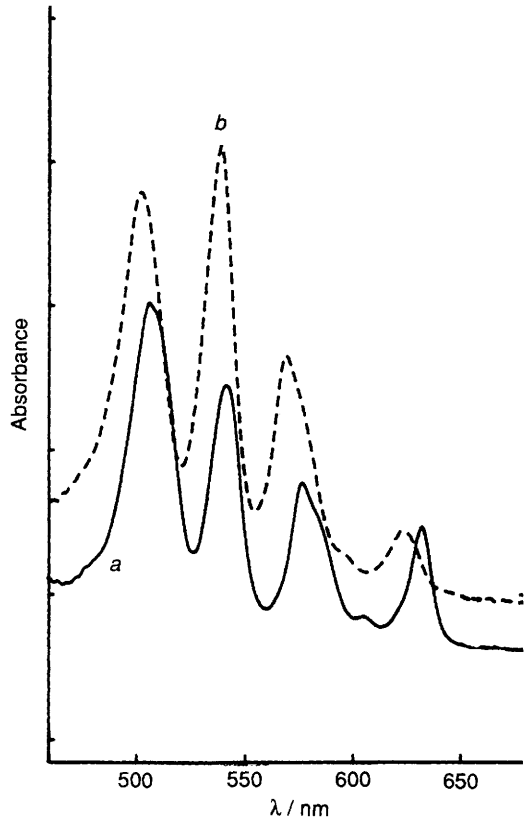


Fig. 1 Optical spectra (460–680 nm region) in CH_2Cl_2 of (*a*) diethynylporphyrin **2**; (*b*) monoethynylporphyrin **3**

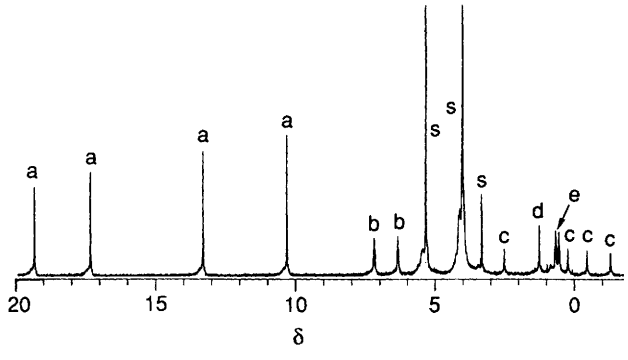
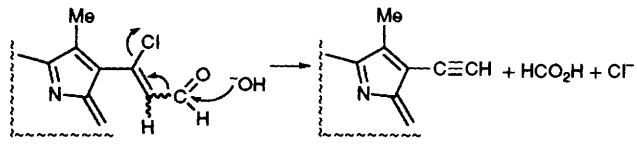


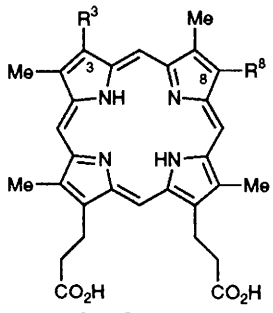
Fig. 2 ^1H NMR spectrum, at 300 MHz in CD_2Cl_2–CD_3OD, of the low spin dicyanoferrihaemin from **12**. Assignments: a, Me; b, CH_2CH_2CO; c, *meso*-5,10,15,20-H; d, C≡CH; e, CH_2CH_2CO; s, solvent.

ties.[3,4] These structural variants of the basic protoporphyrin IX system, their haems and haem proteins, have subsequently been examined using a variety of chemical and spectroscopic techniques, with the intention of building up a series of structure–function relationships, which can be used to interpret data from native heme proteins.

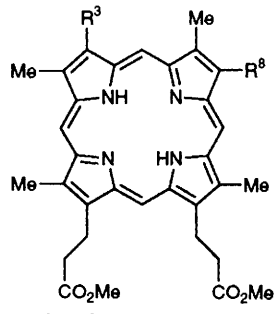
So far as we are aware, diethynyl **2** and monoethynyl (*e.g.* **3**) derivatives of deuteroporphyrin IX dimethyl ester **4** have never been prepared. Ethynylporphyrins have begun to attract considerable attention because of the synthetic potential offered by manipulation of the ethyne functionality. The first *meso*-ethynylporphyrin was prepared by Arnold *et al.* in 1978,[5] and these efforts have very recently been followed up by Anderson,[6] and by Arnold and Nitschinsk.[7,8] The latter authors prepared β-ethynyl substituted porphyrins, and even



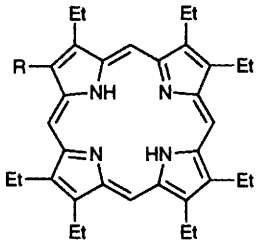
Scheme 1 Proposed mechanism for formation of ethyne function from (1-chloro-2-formylvinyl) with KOH



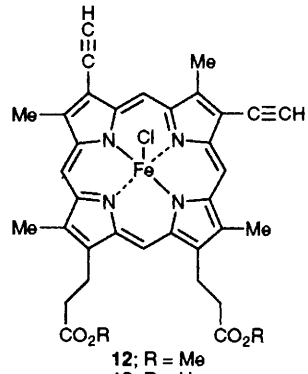
1; $R^3 = R^8 = CH{=}CH_2$



2; $R^3 = R^8 = C{\equiv}CH$
3; $R^3 = H$, $R^8 = C{\equiv}CH$
4; $R^3 = R^8 = H$
5; $R^3 = R^8 = CH{=}CH_2$
6; $R^3 = R^8 = COMe$
7; $R^3 = R^8 = C(Cl){=}CHCHO$
8; $R^3 = H$, $R^8 = COMe$
9; $R^3 = H$, $R^8 = C(Cl){=}CHCHO$



10; R = C(Cl)=CHCHO
11; R = C≡CH



12; R = Me
13; R = H

mentioned[8] a trimethylsilylethynyl deuteroporphyrin obtained using a variant of the palladium method.[9]

In the present paper we report the synthesis of the 3,8-diethynyl derivative **2** of protoporphyrin IX dimethyl ester **5**, and of the corresponding haemin. 3,8-Diacetyldeuteroporphyrin IX dimethyl ester **6** was prepared from the copper(II) complex of deuteroporphyrin IX dimethyl ester **4** using standard Friedel–Crafts methodology.[10] Treatment of **6** with an excess of phosphoryl chloride and *N*-*N*-dimethylformamide (DMF) gave an unoptimized 30% yield of the 3,8-bis(1-chloro-2-formylvinyl) derivative **7**.† Treatment of **7** with KOH in DMF gave a 26% yield of the 3,8-diethynylporphyrin **2** after re-esterification.† We propose the mechanism show in Scheme 1 for this transformation. Fig. 1(*a*) shows the optical

† Note that higher yields are obtained in the monoethynyl series (compounds **3**, **11**).

spectrum of **2**; the ^{1}H NMR spectrum of **2** was unexceptional, and was characterized by the two ethynyl protons at δ 4.21. Similar chemistry using 8-acetyldeuteroporphyrin IX dimethyl ester **8** yielded the 8-(1-chloro-2-formylvinyl)porphyrin **9** (69% yield) and subsequently the monoethynylporphyrin **3** (49%), whereas 2-(1-chloro-2-formylvinyl)-3,7,8,12,13,17,18-heptaethylporphyrin **10** gave a good yield of the monoethynyl-heptaethylporphyrin **11**. Fig. 1(*b*) shows the optical spectrum of porphyrin **3**, and demonstrates the rhodofying effect of the substituent which is cancelled in the diethynylporphyrin **2**.

Treatment of **2** with iron(II) chloride in acetonitrile gave a 92% yield of the haemin chloride dimethyl ester **12**. Fig. 2 displays the low spin dicyano iron(III) ^{1}H NMR spectrum of this derivative. Biological results of the reconstitution of the hydrolysis product **13** with various apoproteins will be reported in due course.

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