Iodination and Heck Alkynylation of 5,15-Diphenylporphyrin. A Convenient Entry to Asymmetrically *meso*-Substituted Porphyrins

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Iodination of 5,15-diphenylporphyrin followed by metallation and palladium(0) catalysed coupling with monosubstituted acetylenes gives zinc(II)-10-(2-substituted-alkynyl)-5,15-diphenylporphyrins.

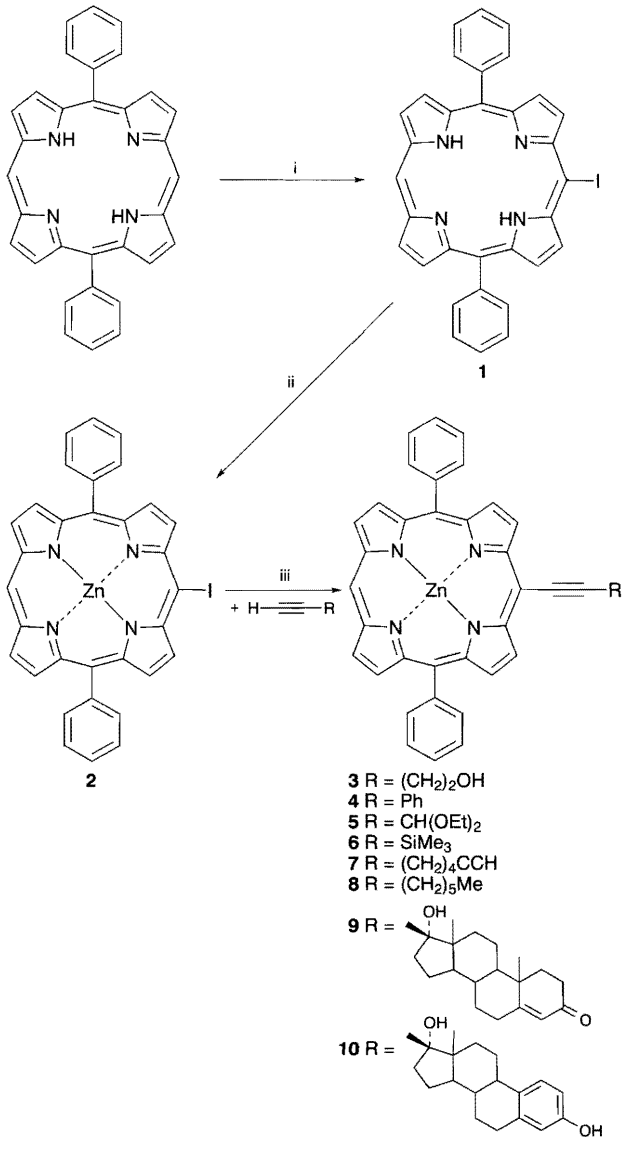
The halogenation of porphyrins has been the subject of many reports; however, while brominations[1,2] and chlorinations[3,4] have been performed successfully for many differently substituted porphyrins, under a variety of experimental conditions, iodinations have proved to be problematic, either yielding unstable products[5] or requiring activation of the porphyrin with highly toxic mercury salts.[6] Failure of simple iodination reactions in the case of octaethyl- and tetraphenyl-porphyrins has been attributed to steric hindrance by the alkyl or phenyl substituents, preventing the large iodinium ion from performing efficient electrophilic attack on the periphery of the porphyrin ring. We believed that elimination of these steric factors, while retaining the electron density of the porphyrin system, would allow 'normal' iodination procedures to be applied to porphyrins.

5,15-Diphenylporphyrin, lacking β-pyrrolic substituents, seemed a good candidate for our initial experiments. Treatment of 5,15-diphenylporphyrin with *N*-iodosuccinimide or bis(trifluoroacetoxy)iodobenzene–iodine in chloroform gave a mixture of iodination products including mono, di and tri substitution, as indicated by TLC and MS analyses, while use of iodine monochloride resulted, unexpectedly, in chlorination of the porphyrin. As the *N*-iodosuccinimide reaction proceeded slowly, over several days, and required considerable excesses of reagent, while iodination with bis(trifluoroacetoxy)iodobenzene–iodine was complete in less than 1 h, the latter system was optimized. Using 1.5 equiv. of bis(trifluoroacetoxy)iodobenzene–iodine (1.2:1) gave monoiodo-5,15-diphenylporphyrin in yields greater than 70% after separation from the contaminating diiodo-5,15-diphenylporphyrin (Scheme 1). NMR examination of the two iodination products revealed that, while the first iodination takes place at one of the two available *meso* positions, the second substitution occurs, not at the remaining *meso* position, but indiscriminately at a β-position resulting in a mixture of regioisomers.

As the 10-iodo-5,15-diphenylporphyrin **1** could be obtained easily, and in high yield, our subsequent investigations into the usefulness of iodinated 5,15-diphenylporphyrin in Pd^0 catalysed alkynylation reactions concentrated on this species. Metal-mediated cross-coupling involving porphyrins has recently been reported using brominated porphyrins and organo-tin and -zinc compounds.[7] There have been no reports of the more facile Heck type coupling[8] of *meso*-iodinated porphyrin with monosubstituted alkynes; however, during the course of this work results of Heck alkynylation on a crude mixture of mono- and di-β-iodinated deuterioporphyrin dimethyl esters has been published.[9]

In order to prevent the possibility of complexation of the metal-free porphyrin with copper or palladium used in the coupling reaction, 10-iodo-5,15-diphenylporphyrin was first converted to its zinc complex.

Zinc(II)-10-iodo-5,15-diphenylporphyrin **2** was treated with a range of monosubstituted alkynes in tetrahydrofuran–triethylamine (50:1) in the presence of catalytic quantities of bis(triphenylphosphine)palladium chloride and copper(I) iodide (Scheme 1). All the alkynes treated in this way reacted smoothly to give the corresponding zinc(II)-10-(2-substituted-alkynyl)-5,15-diphenylporphyrins **3**–**10** in 50–90% yield. The only other major product was unconverted starting material, which could, conveniently, be recovered and used in subsequent coupling reactions. As can be seen from the diversity of substituted alkynes which undergo this reaction, the method is a powerful tool for attaching substituents to a porphyrin through a common acetylenic linkage to give isomerically pure products. The fact that the coupling is carried out under conditions of ambient temperature and pressure also makes it attractive for conjuga-



Scheme 1 *Reagents and conditions*: i, $(F_3CCO_2)_2PhI$–I_2, $CHCl_3$, 25 °C, 1 h; ii, $Zn(OAc)_2 2H_2O$, MeOH–$CHCl_3$, reflux, 16 h; iii, $Pd(PPh_3)_2Cl_2$, CuI, THF–triethylamine, 25 °C, 2 h. All products gave satisfactory spectroscopic and analytical data.

tion of biologically active moieties to porphyrins, as demonstrated by the linking of 17α-ethynyltestosterone and 17α-ethynylestradiol with **2**.

Finally, all the coupled products **3–10** underwent facile demetallation on stirring in a dilute solution of trifluoroacetic acid in dichloromethane (30 mmol dm^{-3}). Work has commenced in our laboratory to extend this new method to include other ethynyl substituted, biologically active substrates, and screen these conjugates as photosensitisers for use in photodynamic therapy.

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