

## First examples of intramolecular Pd(0) catalysed couplings on *ortho*-iodinated *meso*-phenyl porphyrins

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Received (in Cambridge, UK) 8th March 2004, Accepted 8th April 2004

First published as an Advance Article on the web 10th May 2004

Palladium catalysed intramolecular cyclisations on *meso*-phenyl porphyrins give access to a range of substituted porphyrins in which one or two of the phenyl *ortho*-carbons are bonded directly to an adjacent  $\beta$ -pyrrolic position.

Porphyrins with secondary ring systems fused onto the macrocyclic core are of considerable interest due to the effect this has on optical, coordination and redox properties. Synthetic routes which yield these compounds can be divided into two groups: inter- and intramolecular. The former includes participation of the exocyclic double bonds of the porphyrin in Diels Alder reactions,<sup>1</sup> 1,3 dipolar cycloadditions<sup>2</sup> and carbene additions.<sup>3</sup> The second group of reactions often involves attack on an exocyclic double bond by an electrophilic group which is attached to the porphyrin at an adjacent *meso*-position, such reactions have been used to generate purpurins<sup>4</sup> and benzochlorins.<sup>5</sup> Recently, reactions between functional groups on a porphyrin  $\beta$ -position and the *ortho*-carbon of a phenyl ring on the adjacent *meso*-position,<sup>6,7</sup> and the inverse reaction between an *ortho*-functionalised *meso*-phenyl and an unsubstituted  $\beta$ -position,<sup>8</sup> have been reported. The reactions which lead to bond formation between the *ortho*-position of a *meso*-phenyl ring and the porphyrin  $\beta$ -position usually result in the formation of a new, fused six membered ring incorporating a ketonic group, due to the use of formyl and, latterly, acyl chloride groups as electrophiles. Much more rare is the formation of new, fused five membered rings joining the phenyl *ortho*-position directly to an adjacent  $\beta$ -position. A few examples of this kind of fused five membered porphyrin system have been reported,<sup>7,9</sup> but usually as unexpected side products and in low yields.

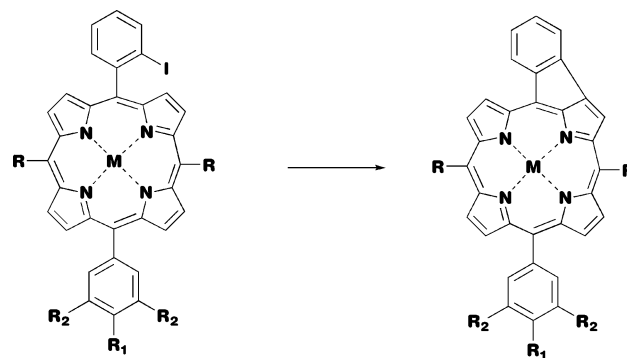
Strangely, although intramolecular reactions between aryl halides and double bonds are well known generally in organic chemistry,<sup>10</sup> and palladium catalysed carbon-carbon bond formations are also well known on porphyrins,<sup>11,12</sup> we are unaware of any reports of intramolecular palladium catalysed ring formation on porphyrins. We now wish to report that this is a versatile and general method for gaining access to porphyrins with *meso*-phenyl rings fused directly to adjacent  $\beta$ -positions, resulting in a new five membered ring fused to the macrocycle.

The required porphyrin scaffolds to develop this novel cyclisation methodology were synthesised either by 2+2 condensation of the appropriate 5-phenyl dipyrromethanes<sup>13</sup> for 5,15-diphenyl porphyrins or by the Adler route<sup>14</sup> for tetraphenyl porphyrin. To facilitate the cyclisation reaction all porphyrins bore at least one *meso*-(2-iodophenyl) group, and to explore the generality of the method several derivatives bearing functionality on the other *meso*-phenyl groups were included.

Initially, all the porphyrins used were complexed with nickel as, generally, intramolecular cyclisation reactions involving the exocyclic double bonds of porphyrins fail on metal free porphyrins. The choice of nickel was primarily to ensure diamagnetic products were formed, which were amenable to NMR analysis. Mono-cyclisation was first attempted on [5-(2-iodophenyl)-15-(4-carbomethoxyphenyl)porphyrinato]Ni(II) **1** using Pd(PPh<sub>3</sub>)<sub>4</sub> (0.1 equiv.) as the source of Pd(0) and K<sub>3</sub>PO<sub>4</sub> (10 equiv.) as base (Fig. 1).<sup>†</sup> Spectral analysis of the product by mass spectrometry indicated the expected mass ion with loss of the iodine atom plus one hydrogen. The NMR spectrum revealed significant loss of symmetry as shown by an increase in the number of signals for the  $\beta$ -hydrogens, to four

doublets and one singlet, as opposed to the normal three doublet pattern found for unsymmetrically phenyl substituted diphenyl porphyrins; however some secondary splitting of the doublets may indicate the presence of seven non-equivalent  $\beta$ -protons, as would be expected. The side of the macrocycle to which the phenyl ring has been bonded is clearly shown by a singlet at 8.17 ppm and two one hydrogen doublets at 8.77 ppm and 9.16 ppm. The UV-visible spectrum exhibited a bathochromic shift (22 nm) and broadening of the Soret band, which was ascribed to deformation of the porphyrin ring caused by formation of the newly fused five membered ring. The deformation caused by the reaction was confirmed by molecular modelling<sup>15</sup> which predicts a significant doming of the aromatic core. The number of Q-bands increased from the two exhibited by the starting material, to four in the cyclised product; an effect which was attributed to alterations in the conformation and conjugate pathway of the chromophore.

Due to the success of this first intramolecular Pd(0) catalysed cyclisation, the generality of the method was explored with a number of related systems. An analogous 5,15-diphenyl porphyrin, [5-(2-iodophenyl)-15-(3,5-dimethoxyphenyl)porphyrinato]Ni(II) **2**, was synthesised and subjected to the same cyclisation conditions. Once again NMR spectral analysis showed the distinctive pattern of  $\beta$ -hydrogen signals indicative of the fused ring product and the signature one hydrogen singlet at 8.17 ppm. MS and UV-visible results were also similar to those found for the initial cyclisation product. Next, in order to investigate the effect of changing the central metal, the Cu(II) complex of 5-(2-iodophenyl)-15-(3,5-dimethoxyphenyl)porphyrin **3** was synthesised and subjected to Pd(0) and base. Although it was not possible to acquire NMR spectra for the product, due to the paramagnetic nature of this metal-porphyrin, both MS and UV-visible analyses indicated that carbon-carbon bond formation between the 2-iodophenyl position and an adjacent porphyrin  $\beta$ -position had occurred. The bathochromic shift of the porphyrin Soret band for this complex (Fig. 2), from 406 nm to 453 nm, was, however, significantly larger than for the nickel analogue, which underwent a more modest shift from



- 1** R = H, R<sub>1</sub> = COOMe, R<sub>2</sub> = H, M = Ni  
**2** R = H, R<sub>1</sub> = H, R<sub>2</sub> = OMe, M = Ni  
**3** R = H, R<sub>1</sub> = H, R<sub>2</sub> = OMe, M = Cu  
**4** R = 4-(COOMe)Ph, R<sub>1</sub> = COOMe, R<sub>2</sub> = H, M = Ni

Fig. 1 Single-intramolecular Pd(0) catalysed cyclisation of di- and tetraphenyl metalloporphyrins in which one phenyl ring bears a 2-iodo substituent.

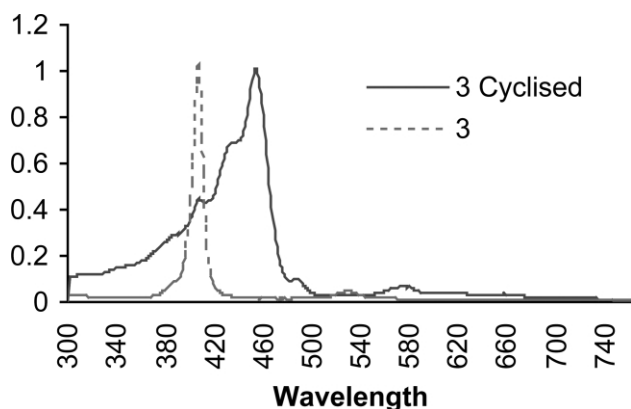


Fig. 2 UV-visible spectrum of **3** before and after cyclisation.

402 nm to 425 nm. Having demonstrated the tolerance of the cyclisation method for alternative substituents on the phenyl ring opposing the 2-iodophenyl ring and different coordinated metals on the 5,15-diphenyl porphyrin system, we decided to attempt the same reaction on [5-(2-iodophenyl)-10,15,20-tri-(4-carbomethoxyphenyl) porphyrinato]Ni(II) **4**. To our great delight the tetraphenyl system underwent cyclisation cleanly and was characterised by NMR, MS and UV-visible spectroscopy. Interestingly, the distinctive one hydrogen singlet found for all examples of these intramolecular cyclisations underwent a significant upfield shift, relative to the diphenyl systems, and was observed at 7.8 ppm, although the  $\beta$ -hydrogens were again found in five different environments. The UV-visible spectrum also showed a bathochromic shift (16 nm) and broadening of the Soret band, while the number of Q bands increased from two to four.

Finally, all the examples above involve mono-cyclisation, however there was clearly a possibility to conduct double cyclisations by subjecting [5,15-di-(2-iodophenyl) porphyrinato]Ni(II) **5** to Pd(0) and base. Although this reaction would lead to a molecule which was predicted, by molecular modelling,<sup>15</sup> to be significantly more strained than the monocyclised products, the reaction was again found to proceed cleanly. MS analysis indicated the success of the reaction, and the NMR spectrum exhibited the characteristic singlet signals from  $\beta$ -hydrogens on the pyrrolic ring newly coupled to the adjacent phenyl ring, however multiples of these resonances indicate the formation of a mixture. The presence of a mixture of isomers resulting from *ortho*-phenyl coupling to the A and B **6** or A and C **7** pyrrolic rings (Fig. 3) is confirmed by the signals arising from the 10, 20 *meso*-hydrogens which show three signals between 9.93 and 9.95 ppm in a 2:1:1 ratio. The UV-visible

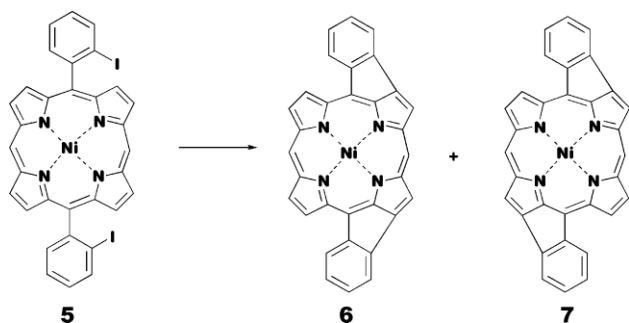


Fig. 3 Double Pd(0) catalysed cyclisation of [5,15-di-(2-iodophenyl) porphyrinato]Ni(II).

spectrum for the mixture showed the now familiar broadening and bathochromic shift of the Soret band, from 403 to 424 nm, coupled with an increase in the number of Q bands from two for the starting material to four in the product. Despite repeated attempts to chromatographically separate the A,B **6** and A,C **7** isomers resulting from the double cyclisation, this has so far proved impossible due to their virtually identical  $R_f$  values.

Yields for all cyclisation reactions performed varied between 36% for the double cyclised products **6,7** and 44% for mono-cyclised product **2**, however the only other major product was starting material which could easily be recovered and used in subsequent cyclisations. Typically, cyclisations were performed on a 30–50 mg scale.

Finally, we can report that all attempts to perform the same Pd(0) catalysed intramolecular cyclisations using the 2-bromophenyl analogues under the conditions described here met with failure, indicating a requirement for the more reactive iodo species.

The authors wish to thank the Wellcome Trust (059572, 066948), BBSRC (21/E12509) and the Leverhulme Trust (F/00181H) for financial support. We also thank Dr Adam Bridgeman for molecular modelling of fused porphyrins and the EPSRC Mass Spectrometry Service, Swansea for analyses. SF thanks EPSRC for a studentship and P. Vlachos for valuable discussions.

## Notes and references

† General method: To a stirred slurry of  $K_2PO_4$  (10 equiv.) in anhydrous DMF (20 ml) was added porphyrin (1 equiv.) and  $Pd(PPh_3)_4$  (0.1 equiv.). The reaction was kept under a nitrogen atmosphere at reflux for 24 hours and protected from light. After completion, the solvent was removed *in vacuo* and the residue was dissolved in  $CH_2Cl_2$ . This solution was washed with a saturated aqueous solution of  $NaHCO_3$ , then brine, and the organic layer was finally dried over anhydrous magnesium sulfate. The solvent was evaporated and the crude product purified by flash chromatography to yield a green solid.

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