

## A New Approach to the Synthesis of Unsaturated $\beta$ -Substituted-*meso*-Tetraphenylporphyrins

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**Abstract:** Treatment of nickel (II) complexes of  $\beta$ -diazonium-*meso*-tetraphenylporphyrin salts with  $\alpha,\beta$ -unsaturated carbonyl compounds, in the presence of palladium acetate, affords the corresponding unsaturated  $\beta$ -substituted porphyrin.

The understanding of the key role of porphyrins in biological functions such as photosynthesis, catalytic oxidative transformations, transportation and storage of molecular oxygen has been greatly assisted by studies using synthetic model porphyrin macrocycles.

*Meso*-Tetraphenylporphyrin (TPP) **1** has been an ideal model for those studies since it is easily prepared in good yields. Its lack of functionalization is being overcome by the intensive work of several research groups.<sup>1-5</sup> In particular the methodology used to introduce unsaturated substituents at a  $\beta$ -position of that macrocycle has been mainly based on Wittig reactions, through an aldehyde functionality<sup>2,3</sup> introduced in the macrocycle or in a more recent version by using a porphyrinic phosphonium salt.<sup>4</sup> Palladium (II) catalyzed carbon-carbon bond formations between  $\beta$ -bromoTPP and a series of terminally substituted acetylenic derivatives have also been reported.<sup>5</sup>

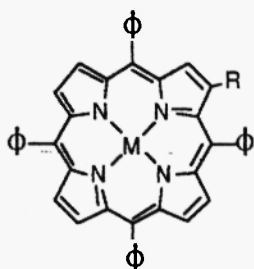
In previous work<sup>1a,1b</sup> we reported an efficient synthesis of  $\beta$ -alkoxy-*meso*-tetraphenylporphyrin derivatives *via* the diazotization of copper  $\beta$ -amino-*meso*-tetraphenylporphyrin **2** (M=Cu), followed by addition of the corresponding alcohol. Here we describe our results on a new approach, based in the Heck reaction of arenediazonium salts,<sup>6</sup> for the introduction of unsaturated groups in the  $\beta$ -position of **1**.

Diazotization of nickel  $\beta$ -amino-*meso*-tetraphenylporphyrin **2** (M=Ni), in tetrahydrofuran, with sodium nitrite and sulfuric acid, followed by the *in situ* addition of methyl acrylate and palladium (II) acetate afforded, after work up and preparative chromatography, the desired acrylate derivative **3** in 39% yield.<sup>7</sup> This compound, as the *E* isomer, was characterized by UV/VIS, mass spectrometry and <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy.<sup>8</sup> A minor product, with a smaller R<sub>f</sub> and a UV/VIS spectrum typical of a metalloporphyrin, was also isolated in 3% yield, which was identified as compound **4**. This compound can be obtained in higher yields

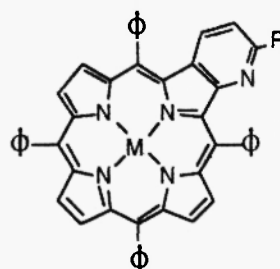
(18-20%) if traces of moisture are present, as in the case when methyl acrylate is previously washed with a basic aqueous solution to remove the stabiliser; however in these cases the yields of the derivative **3** decrease to 20-24%. The structure of this hydroxy derivative **4** was established by MS [(FAB+) (parent ion at  $m/z = 772$ )], and by a detailed analysis of the  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^1\text{H}$ - $^1\text{H}$  COSY and  $^1\text{H}$ - $^1\text{H}$  COSYLR NMR spectra.<sup>9</sup> In particular, the  $^1\text{H}$  NMR spectrum in the aliphatic region showed the presence of two double doublets at  $\delta$  2.71 and 2.82 ppm corresponding to the  $\text{CH}_2$  protons and a doublet at  $\delta$  3.18 ppm and another broad one at  $\delta$  5.15 ppm assigned, respectively, to the  $\text{OH}$  and  $\text{CH}$  protons, respectively. From the COSYLR experiment it was possible to observe the correlation between the  $\text{CH}$  proton of the aliphatic chain and the the  $\beta$ -pyrrolic H-2; these results also agree with structure **4**.

Our studies were extended to the synthesis of the propenal **5** and methyl vinyl ketone **8** derivatives, using similar reaction conditions. When the reaction was performed with propenal, after the usual work up procedure, three compounds were isolated by preparative thin layer chromatography. The less polar one was obtained in 24 % yield, and identified by UV/VIS, mass spectrometry,  $^1\text{H}$  and  $^{13}\text{C}$  NMR as being compound **5**.<sup>10</sup> The second one, just following derivative **5**, was obtained in 23 % yield and showed a parent ion at  $m/z = 727$  (two more hydrogens than the propenal derivative) and analysis by  $^1\text{H}$  and  $^{13}\text{C}$  NMR led us to establish the structure shown as **6**.<sup>11</sup> The aliphatic region showed one double triplet at  $\delta$  2.79 ppm and one triplet at  $\delta$  3.06 ppm corresponding, respectively, to the  $\alpha$  and  $\beta$   $\text{CH}_2$  protons to the carbonyl group. In the aromatic region a singlet at  $\delta$  8.47 ppm and a triplet at  $\delta$  9.63 ppm were assigned to the  $\beta$ -pyrrolic H-2 and to the  $\text{CHO}$  proton, respectively. The third compound, isolated in 6% yield, was identified as the fused pyridinoporphyrin **7**.<sup>12</sup>

The reaction with methyl vinyl ketone afforded compound **8**, its saturated analogue **9** and also the fused pyridinoporphyrin **10** in, respectively, 48%, 3% and 7% yields. The formation of the fused pyridinoporphyryns **7** and **10** can be accounted for by reaction of unchanged aminoporphyrin with the  $\alpha, \beta$ -unsaturated derivative.<sup>12</sup> The formation of the reduced products when propenal and methyl vinyl ketone are used can be envisaged by formation, in acidic medium, of an enolate from the organopalladium intermediate.<sup>13</sup>



- 1** M=2H, R=H  
**2** M=Cu or Ni, R=NH<sub>2</sub>  
**3** M= Ni, R= CH=CHCO<sub>2</sub>Me  
**4** M=Ni, R=CH(OH)CH<sub>2</sub>CO<sub>2</sub>Me  
**5** M=Ni, R= CH=CHCHO  
**6** M=Ni, R= CH<sub>2</sub>CH<sub>2</sub>CHO  
**8** M=Ni, R= CH=CHCOCH<sub>3</sub>  
**9** M=Ni, R= CH<sub>2</sub>CH<sub>2</sub>COCH<sub>3</sub>



- 7** M=Ni, R=H  
**10** M=Ni, R=CH<sub>3</sub>

The present work describes a new route based on the Heck reaction which allows introduction of unsaturated substituents in a  $\beta$ -position of *meso*-tetraphenylporphyrin derivatives using the corresponding diazonium salt.

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  7. **Typical procedure:** Sodium nitrite (4 mg, 0.64 mmol) and concentrated sulfuric acid (0.1 ml) were added to a tetrahydrofuran solution (10 ml) of Ni (II)  $\beta$ -NH<sub>2</sub>TPP (25 mg, 0.04 mmol), and the mixture was stirred until a change of colour from violet to green was observed (~ 45 min). After this period, palladium acetate (4 mg) and the  $\alpha,\beta$ -unsaturated derivative was added (8 mmol) and the reaction mixture stirred for 2 h (a colour change from green to reddish was observed). Then the solution was neutralised with diluted aqueous sodium carbonate and extracted with dichloromethane (2 x 100 ml). The organic layer was washed with water, dried (sodium sulfate) and evaporated to dryness. The residue was taken in dichloromethane and chromatographed on preparative thin layer chromatography, eluting in each case with different light petroleum:dichloromethane mixtures, affording the new products.
  8. Spectroscopic data for **3**: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  (ppm) 3.74 (s, 3H, OCH<sub>3</sub>), 6.43 (d, 1H, *J* 15.6 Hz, -CH=CH-CO-), 7.30 (d, 1H, *J* 15.6 Hz, -CH=CH-CO-), 7.65-7.67 (m, 12H, *m*-H and *p*-H), 7.87-7.99 (m, 8H, *o*-H), 8.66-8.73 (m, 6H, H-7,8,12,13,17,18), 8.89 (d, *J* 8.4 Hz, H-2); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  (ppm) 51.3, 118.0, 118.7, 118.9, 119.1, 119.2, 127.0, 127.0, 127.3, 127.8, 128.0, 128.2, 128.5, 131.9, 132.1, 132.5, 132.6, 132.6, 132.7, 133.0, 133.3, 133.6, 139.2, 140.1, 140.2, 140.3, 140.4,

- 140.4, 142.3, 142.9, 142.9, 143.0, 143.3, 143.4, 167.2; UV- Vis ( $\text{CHCl}_3$ )  $\lambda_{\text{max/nm}}$  ( $\log \epsilon$ ), 427 (5.26), 538 (4.15) and 573 (3.89); MS (FAB<sup>+</sup>)  $m/z = 754$  (M<sup>+</sup>).
9. Spectroscopic data for 4: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 2.71 (dd, 1H,  $\text{CH}_2$ ,  $J$  9.0 and 16.7 Hz), 2.82 (dd, 1H,  $\text{CH}_2$ ,  $J$  2.9 and 16.7 Hz), 3.18 (d, 1H, OH,  $J$  2.8 Hz) 3.65 (s, 3H,  $\text{OCH}_3$ ), 5.15 (d broad, 1H, CH,  $J$  9.0 Hz), 7.62-8.03 (m, 20H, *o*-H,*m*-H and *p*-H), 8.64, 8.66, 8.68 and 8.71 (4 d, 4H,  $J$  5.0 Hz, H-7,8,17,18) 8.71 (s, 2H, H-12,13), 8.89 (s, 1H, H-2); <sup>13</sup>C NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 43.6, 51.7, 65.7, 117.7, 118.5, 118.9, 119.2, 127.0, 127.5, 127.8, 127.8, 128.5, 128.8, 131.9, 132.2, 132.3, 132.5, 132.6, 132.7, 132.9, 133.0, 133.8, 138.0, 140.4, 140.5, 140.6, 142.3, 142.5, 142.6, 142.7, 143.3, 147.8, 172.6; UV-Vis ( $\text{CHCl}_3$ )  $\lambda_{\text{max/nm}}$  ( $\log \epsilon$ ), 416 (5.35), 529 (4.20); MS (FAB<sup>+</sup>)  $m/z = 772$  (M<sup>+</sup>).
10. Spectroscopic data for 5: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 6.74 (dd, 1H,  $-\text{CH}=\text{CHCHO}$ ,  $J$  7.9 and 15.5 Hz) 6.95 (d, 1H,  $-\text{CH}=\text{CHCHO}$ ,  $J$  15.5 Hz), 7.61-7.76 (m, 12H, *m*-H and *p*-H) 7.90-7.99 (m, 8H, *o*-H), 8.68-8.75 (m, 4H, H-7,8,17,18), 8.72 (s, 2H, H-12,13), 8.93 (s, 1H, H-2), 9.15 (d, 1H,  $-\text{CHO}$ ,  $J$  7.9 Hz); <sup>13</sup>C NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 118.4, 119.1, 119.2, 119.8, 127.0, 127.4, 127.9, 128.1, 128.7, 128.9, 132.3, 132.7, 132.8, 132.9, 133.0, 133.5, 133.6, 139.1, 139.2, 140.1, 140.2, 140.3, 140.5, 142.4, 143.3, 143.3, 148.4, 194.0; UV- Vis ( $\text{CHCl}_3$ )  $\lambda_{\text{max/nm}}$  ( $\log \epsilon$ ), 431 (5.14), 546 (4.07), 585 (3.97); MS (FAB<sup>+</sup>):  $m/z = 725$  (M+H)<sup>+</sup>.
11. Spectroscopic data for 6: <sup>1</sup>H NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 2.79 (dt, 2H,  $-\text{CH}_2\text{CH}_2\text{CHO}$ ,  $J$  1.5 and 7.7 Hz), 3.06 (t, 2H,  $-\text{CH}_2\text{CH}_2\text{CHO}$ ,  $J$  7.7 Hz), 7.61-7.71 (m, 12H, *m*-H and *p*-H) 7.88-7.99 (m, 8H, *o*-H), 8.47 (s, 1H, H-2), 8.66-8.73 (m, 4H, H-7,8,17,18), 8.67 (s, 2H, H-12,13), 9.63 (t, 1H,  $-\text{CHO}$ ,  $J$  1.5 Hz); <sup>13</sup>C NMR ( $\text{CDCl}_3$ )  $\delta$  (ppm) 44.5, 68.1, 117.4, 118.1, 118.8, 119.3, 126.9, 127.3, 127.8, 128.4, 128.8, 130.9, 131.8, 132.1, 132.2, 132.3, 132.6, 133.6, 139.3, 140.6, 140.7, 140.8, 141.9, 142.1, 142.3, 142.4, 142.6, 143.3, 145.5, 201.8; UV- Vis ( $\text{CHCl}_3$ )  $\lambda_{\text{max/nm}}$  ( $\log \epsilon$ ), 415 (5.28), 532 (4.03); MS (FAB<sup>+</sup>):  $m/z = 727$  (M+H)<sup>+</sup>.
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