



# Carbonyl ylide 1,3-dipolar cycloadditions with porphyrins

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**Abstract**—Carbonyl ylides react with tetraarylporphyrins to afford the corresponding [3+2] tetrahydrofuran cycloaddition products in moderate yields. © 2002 Published by Elsevier Science Ltd.

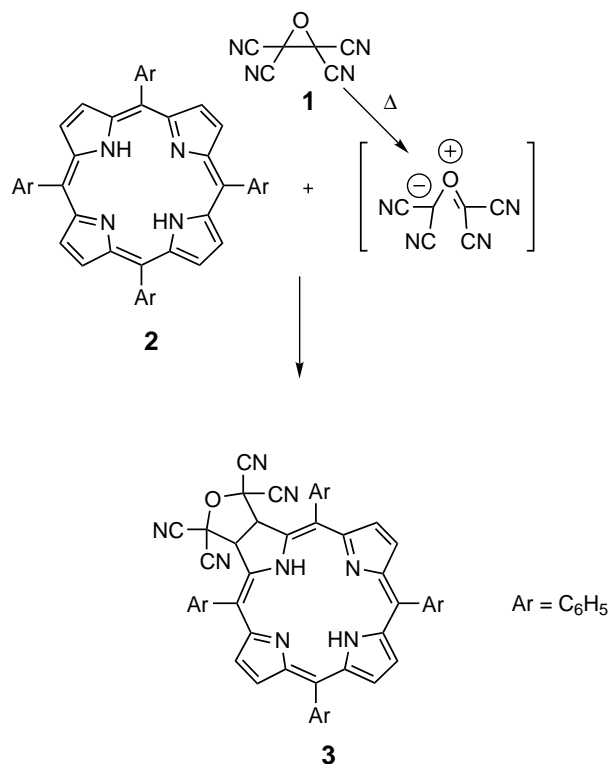
1,3-Dipolar [3+2] cycloadditions are an effective method for the synthesis of five-membered heterocycles.<sup>1</sup> Carbonyl ylides undergo 1,3-dipolar cycloadditions with a variety of dipolarophiles in the synthesis of tetrahydrofuran derivatives.<sup>1</sup> Electron deficient carbonyl ylides are known to react with many dipolarophiles, including aromatic systems<sup>2</sup> and non-stabilized carbonyl ylides have also been shown to react with a variety of dipolarophiles, including electron deficient, electron rich- and hetero-dipolarophiles.<sup>3</sup>

Recent research into the synthesis of chlorins and bacteriochlorins from porphyrins has been intense, as many chlorins have been identified as useful agents for photodynamic therapy (PDT).<sup>4</sup> This stems from their preferable light absorption characteristics, since they absorb light strongly at wavelengths where human tissue does not.<sup>4</sup> Carbonyl ylides were thus investigated for their ability to react with various porphyrins in order to synthesize chlorins and bacteriochlorins. To the best of our knowledge, there has been no report on the reaction of carbonyl ylides with porphyrins. The 1,3-dipolar cycloaddition reaction between azomethine ylides<sup>5</sup> and sugar nitrones<sup>6</sup> with porphyrins have been reported by Cavaleiro's group.

We now report that the reaction of tetracyanoethylene oxide (TCNEO, **1**) with tetraphenylporphyrin (TPP, **2**) in refluxing toluene gives the corresponding cycloadduct **3** in moderate yield (Scheme 1). We also note that the reaction of  $\alpha,\alpha'$ -dichloromethylether **5** with tetrakis(pentafluorophenyl)porphyrin **6** in the presence of  $\text{PbCl}_2$ , Mn and NaI at rt gives the corresponding

tetrahydrofuran cycloadduct **7** also in moderate yield (Scheme 2).

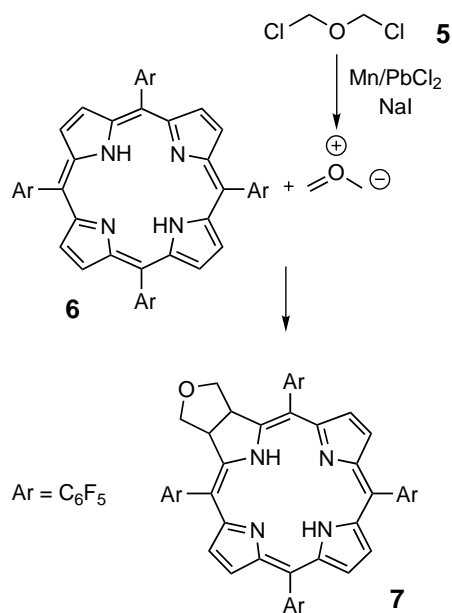
It was found that TCNEO undergoes first order thermal electrocyclic ring opening to the corresponding carbonyl ylide in refluxing toluene, which then reacts via 1,3-dipolar cycloaddition with a variety of dipolarophiles to form the [3+2] cycloadducts.<sup>2</sup> When **1** and **2** were refluxed together for 1 h, followed by concentration under reduced pressure and purification by



Scheme 1.

**Keywords:** carbonyl ylide; cycloadditions; porphyrins; chlorins.

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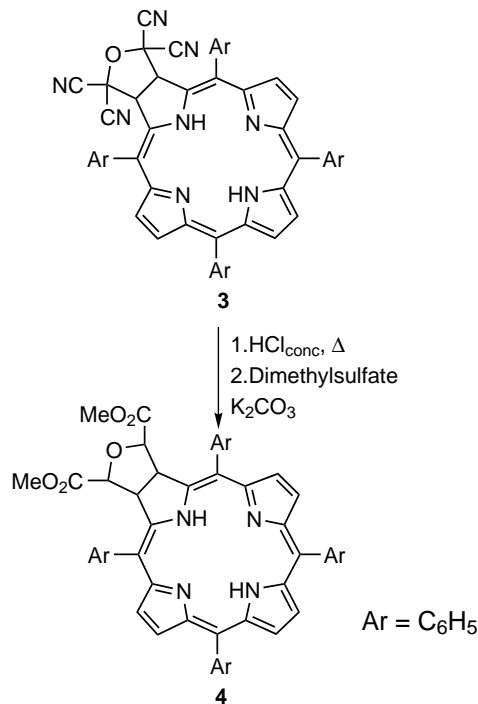


Scheme 2.

preparatory tlc on 2 mm silica gel plates (50% CH<sub>2</sub>Cl<sub>2</sub>/hexane), the product **3**<sup>7</sup> was obtained in 20% yield. In the interests of manipulating the physical properties, hydrolysis of the cyano functionalities was attempted. Refluxing **3** in conc. HCl for 8 h, followed by methylation with dimethylsulfate and K<sub>2</sub>CO<sub>3</sub> gave compound **4**<sup>8</sup> in a 10% yield (Scheme 3).

The non-substituted carbonyl ylide was obtained when tetrakis(pentafluorophenyl)porphyrin (**6**) was added to a suspension of PbCl<sub>2</sub>, Mn, NaI and **5** in THF,<sup>9</sup> which was then allowed to stir under an N<sub>2</sub> atmosphere. The reaction was quenched with water, and the mixture separated with CH<sub>2</sub>Cl<sub>2</sub>, and washed with water. After drying over MgSO<sub>4</sub> and purification by preparatory tlc on 2 mm silica gel plates (50% CHCl<sub>3</sub>/hexane), the product **7**<sup>10</sup> was contained in 38% yield.

The compounds synthesized in the carbonyl ylide 1,3-dipolar cycloaddition reactions are chlorins, and exhibit similar electronic absorption spectra (Fig. 1). The small



Scheme 3.

differences in the highest wavelength band (~650) is accounted for by steric and electronic effects.<sup>11</sup>

The difference in reactivity of the porphyrins (**2** and **6**) towards the two carbonyl ylides is not unexpected. Carbonyl ylides are type I dipoles.<sup>12</sup> These are often referred to as nucleophilic dipoles as they tend to react most efficiently with electron rich dipolarophiles. In the case of the non-stabilized carbonyl ylide, it seems to react according to this rule, as a cycloadduct is formed with the relatively electron deficient **6** but no reaction is observed with the relatively electron rich **2**. On the other hand, the carbonyl ylide formed by the electrocyclic ring opening of **1** reacts with **2**, but not at all with **6**. This at first glance would seem to be contradictory to the general rule, but there are examples in the literature

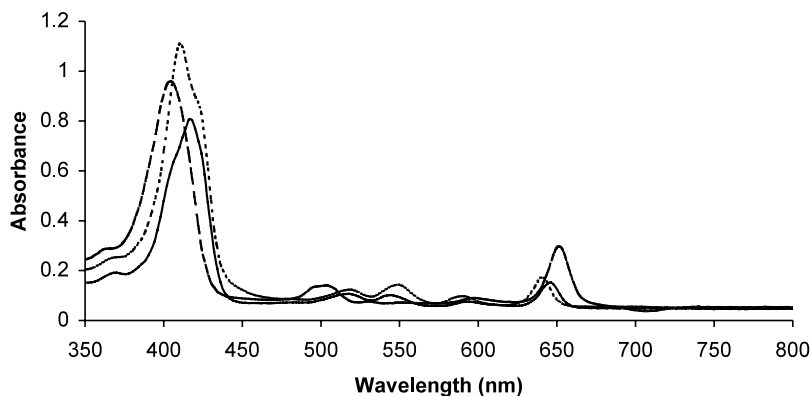


Figure 1. Optical spectra (CH<sub>3</sub>Cl<sub>3</sub>) of compounds **3** ---, **4** —, **7** ----.

of class I 1,3-dipoles, that once substituted with electron withdrawing groups, will undergo ‘inverse electron demand’, and react with electron rich dipolarophiles.<sup>13</sup>

In conclusion, we have developed a novel method for the synthesis of chlorins. This method is potentially useful for the synthesis of molecules for use in PDT. We have also shown that the substituents on the phenyl groups of tetraarylporphyrins effect its reactivity with 1,3-dipoles.

### Acknowledgements

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7. Spectroscopic data for compound **3**. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm) δ=8.70 (d, *J*=4.89 Hz, 2H), 8.50 (s, 2H), 8.38 (d, *J*=4.89 Hz, 2H), 8.13–7.66 (m, 20H), 6.00 (s, 2H), –2.05 (s, 2H). UV–vis (CHCl<sub>3</sub>) λ<sub>max</sub> (rel. intensity) 416 (1.0), 514 (0.14), 554 (0.18), 586 (0.10), 642 (0.22). LRMS (LSIMS) 759 *m/z* (MH<sup>+</sup>=100%).
8. Spectroscopic data for compound **4**. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm) δ=8.60 (d, *J*=4.89 Hz, 2H), 8.45 (s, 2H), 8.28 (d, *J*=4.89 Hz, 2H), 8.13–7.66 (m, 20H), 6.02 (s, 2H), 4.92 (s, 2H), 3.53 (s, 6H), –1.96 (s, 2H). UV–vis (CHCl<sub>3</sub>) λ<sub>max</sub> (rel. intensities) 416 (1.00), 518 (0.10), 544 (0.09), 592 (0.07), 646 (0.14). MS (LSIMS) dev. in ppm for mass calculated for C<sub>53</sub>H<sub>20</sub>F<sub>20</sub>N<sub>5</sub>: 0.30, found 775.29228 *m/z* (MH<sup>+</sup>=100%).
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10. Spectroscopic data for compound **7**. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, ppm) δ=8.70 (d, *J*=4.90 Hz, 2H), 8.47 (s, 2H), 8.38 (d, *J*=4.90 Hz, 2H), 5.33 (t, *J*=4.36 Hz, 2H), 4.20 (t, *J*=8.17 Hz, 2H), 4.20 (t, *J*=8.17 Hz, 2H), 3.92 (dd, *J*=4.36 Hz and 8.17 Hz, 2H), –1.50 (s, 2H). UV–vis (CHCl<sub>3</sub>) λ<sub>max</sub> (rel. intensities) 414 (1.00), 506 (0.03), 603 (0.01), 656 (0.128). LRMS (LSIMS) 1019 *m/z* (MH<sup>+</sup>=100%).
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