

The First Example of Oxidative Nucleophilic Substitution of Hydrogen in *meso*-Aryl Ring of the 5,10,15,20-Tetraphenylporphyrin Derivatives

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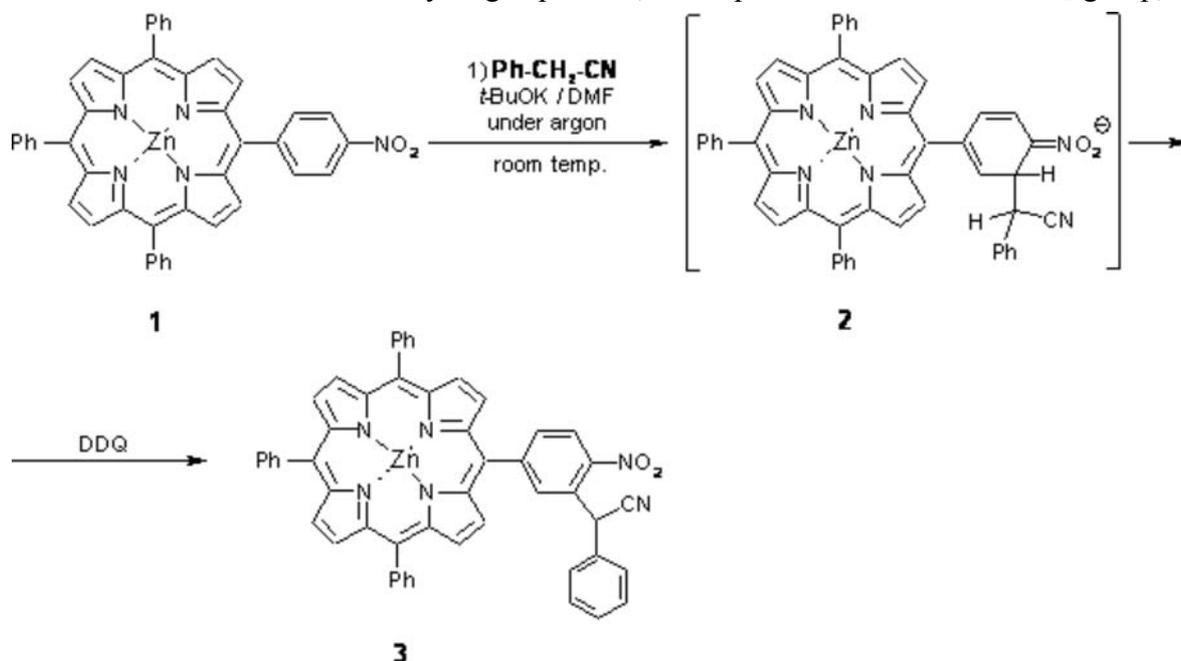
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Abstract:

A synthesis of [2-nitro-5-(10,15,20-triphenylporphyrin-5-yl)-phenyl]phenyl-acetonitrile zinc complex by the reaction of the respective nitroporphyrin with the anion of benzyl cyanide, followed by addition of DDQ, is described. This is the first example of this type of process in the nitrophenyl side ring of *meso*-tetraarylporphyrin derivatives.

The synthesis of unsymmetrical, double functionalized in *meso*-aryl ring, porphyrins is of significant importance due to their potential application as sensitizers in photodynamic cancer therapy (PDT).¹ Amongst other methods, a very attractive one seems to be oxidative nucleophilic substitution of hydrogen (ONSH²) in nitrophenyl moiety of the respective starting porphyrin. Herein, we present the first example of this type of functionalization in the reaction of 5-(4-nitrophenyl)-10,15,20-triphenylporphyrin zinc complex³ with phenylacetonitrile carbanion (in DMF, at room temperature) followed by addition of DDQ. This leads to the substitution of hydrogen product, in the position *ortho*- to the NO₂ group, in 35% yield.



Scheme 1

To a stirred solution of *t*-BuOK (71 mg, 0.63 mmol) in anhydrous DMF (5 mL, under argon), a solution of 5-(4-nitrophenyl)-10,15,20-triphenylporphyrin zinc(II)³ (**1**; 50 mg, 0.069 mmol) and benzyl cyanide (19 mg, 0.16 mmol) in DMF (3 mL) was added dropwise *via* syringe at room temperature during *ca* 2 min. After an additional 2 min of stirring, DDQ (23 mg, 0.10 mmol) was added in a one portion and the mixture

was stirred for 3 min. Then, the mixture was poured into 3% HCl containing ice (80 mL). The precipitate was filtered, washed with water (3×15 mL), and then dissolved in CHCl_3 (40 mL). After drying with anhydrous MgSO_4 and evaporation of the solvent, the residue was chromatographed (silica gel 230-400 mesh; eluent: CHCl_3 / *n*-hexane, 2: 1) to give: starting porphyrin **1** – 15.4 mg (31%), and product **3** – 13.9 mg (24%; 35% for recovered substrate).

Melting point: > 300 °C

IR (CH_2Cl_2 , cm^{-1}): 2246 (CN), 1598, 1583, 1525 (asym. NO_2), 1487, 1441, 1340 (sym. NO_2).

^1H NMR (CDCl_3 , 200 MHz): 9.04 (d, $J = 4.8$ Hz, 1 H, H^β -pyrrole), 8.99-8.94 (m, 5 H, H^β -pyrrole), 8.89 (d, $J = 4.8$ Hz, 1 H, H^β -pyrrole), 8.69 (d, $J = 4.8$ Hz, 1 H, H^β -pyrrole), 8.65 (d, $J = 1.6$ Hz, 1 H, H-2 of H-Ar(NO_2)), 8.49 (part of AB system, $J = 8.3$ Hz, 1 H, H-5 of H-Ar(NO_2)), 8.40 (part of AB system coupled with another proton, $J = 8.3$ Hz, 1.6 Hz, 1 H, H-6 of H-Ar(NO_2)), 8.28-8.16 (m, 6 H, H-Ph), 7.86-7.68 (m, 9 H, H-Ph), 7.58-7.31 (m, 5 H, $\text{CH}(\text{CN})\text{Ph}$), 6.54 (s, 1 H, $\text{CH}(\text{CN})$).

UV-VIS (CHCl_3): λ_{max} ($\log \varepsilon$): 589.5 (3.79), 548.0 (4.47), 510.5 (3.70), 418.5 (5.55, Soret band), 348.0 nm (4.20).

MS (EI), m/z (% rel. int.): 836 (1.0, $\text{M}^{+\bullet}$), 810 (0.9, M-CN), 733 (0.5), 678 (2), 677 (4), 676 (3), 675 (4), 674 (1.1), 77 (41), 44 (100, CO_2^+).

MS (ESI), m/z (% rel. int.): 842 (11), 841 (16), 840 (46), 839 (50), 838 (80), 837 (57), 836 (100) [isotopic M^+]. The molecular formula was confirmed by comparing the theoretical and experimental isotope patterns for the M^+ ion ($\text{C}_{52}\text{H}_{32}\text{N}_6\text{O}_2\text{Zn}$) – found to be identical within the experimental error limits.

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