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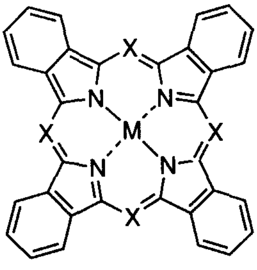
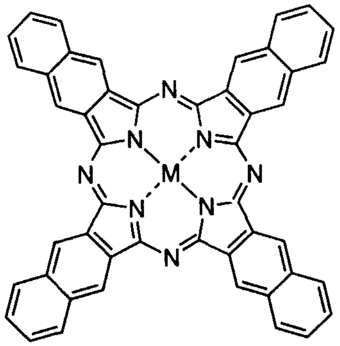
Synthesis of Dinaphthoporphyrins from Dihydronaphtho[1,2-c]pyrroles

Timothy D. Lash* and Tracy J. Roper
Department of Chemistry, Illinois State University, Normal, Illinois 61790-4160, U.S.A.

Abstract: *Porphyrins with two fused dihydronaphtho units on the opposite or adjacent pyrrole rings have been prepared by the MacDonald condensation or by the cyclization of suitably substituted a,c-biladienes; dehydrogenation with 2 equivalents of DDQ afforded the corresponding dinaphthoporphyrins in excellent yields.*

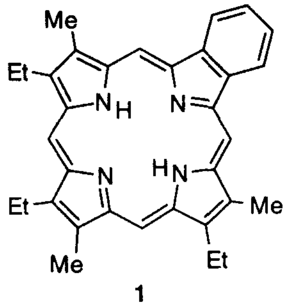


Phthalocyanine X = N
Tetrabenzoporphyrin X = CH

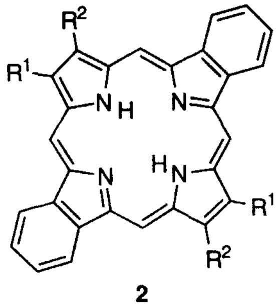


Naphthocyanine

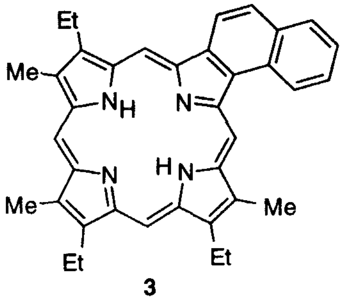
The phthalocyanines were discovered by accident over sixty years ago when phthalic anhydride was heated with ammonia inside an iron vessel.[1] Since that time, these metal chelates have become one of the most studied classes of industrial pigments[2] and have been shown to have a multitude of applications. The pioneering work of R.P. Linstead and his collaborators led to the investigation of many related macrocyclic systems,[3] including the naphthocyanines[4] and tetrabenzoporphyrins.[5,6] Mono- and dibenzoporphyrins (**1** and **2**, respectively) were synthesized as standards for the analysis of sedimentary porphyrins,[7] but otherwise systems of this type have been little studied. Porphyrinoid pigments with red shifted uv-vis absorption bands are currently receiving considerable attention due to their potential application as photosensitizers in photodynamic therapy (PDT).[8] Hybrid structures such as **1**-**3** might be suitable for this purpose, although many other applications (near infrared dyes, fluorescent probes, geochemical standards, etc.) can be envisaged. Recently, due to the potential value of these highly conjugated porphyrin systems, improved syntheses of monobenzoporphyrins (**1**),[9] dibenzoporphyrins (**2**)[10] and naphthoporphyrins (**3**)[9] have been developed. These studies have now been extended to the first syntheses of dinaphthoporphyrins.



1

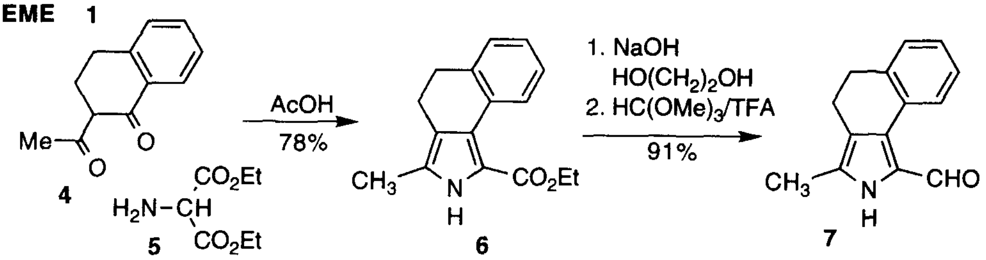


2



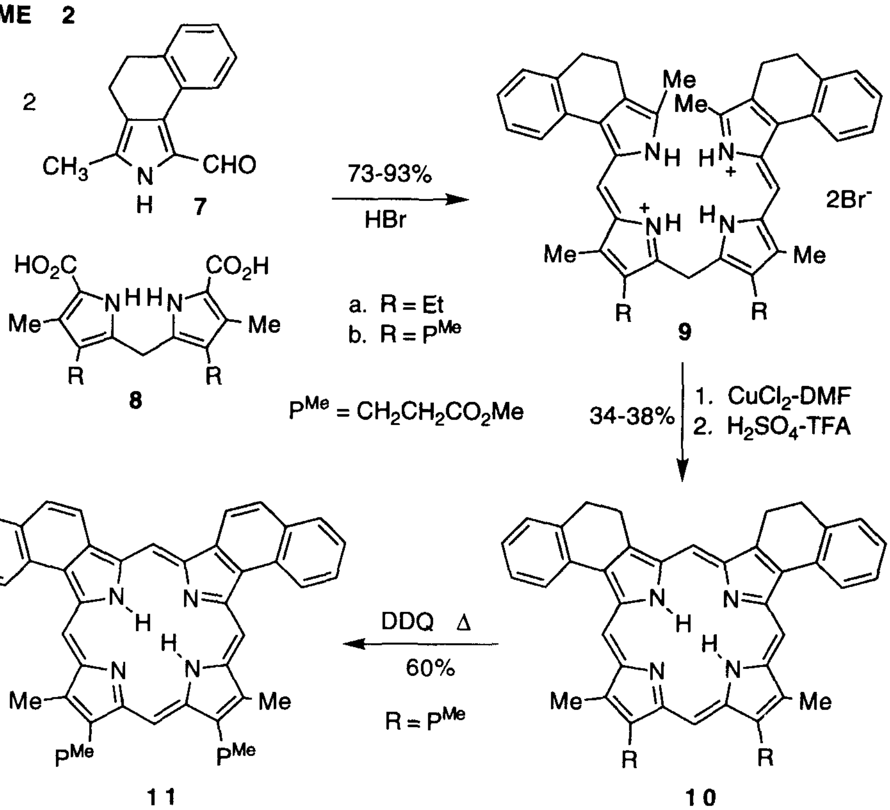
3

SCHEME 1



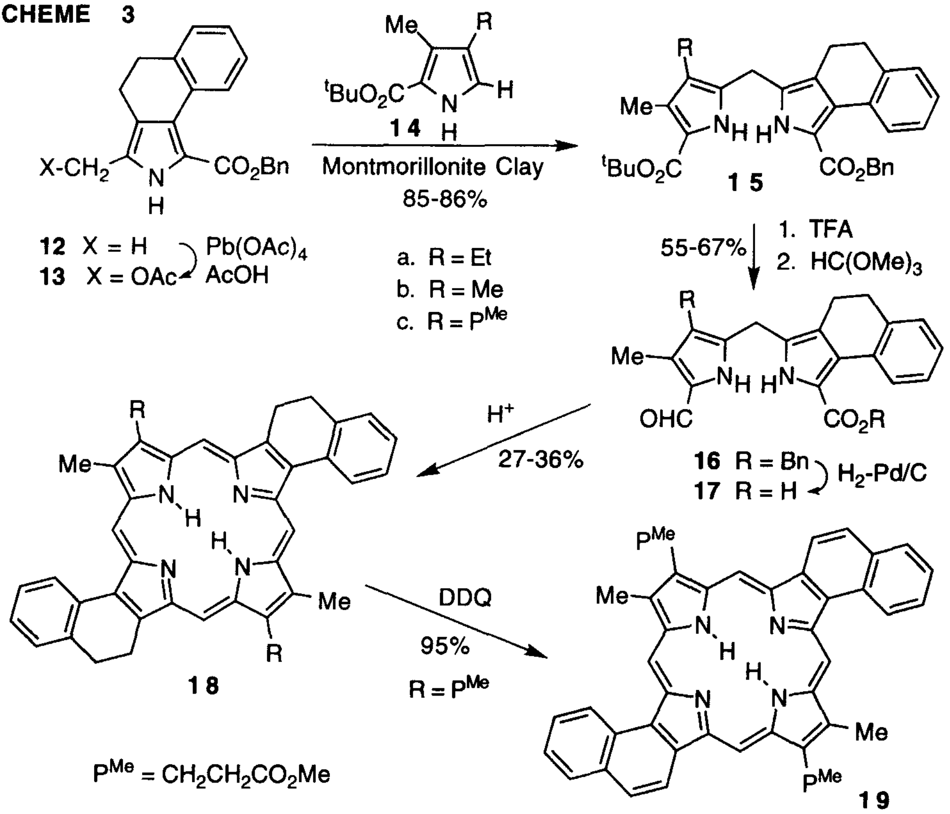
The synthesis of dinaphthoporphyrins was reliant upon the availability of pyrrolic precursors bearing the required naphthalene subunit. Readily available 2-acetyl-1-tetralone (**4**) was found to condense with diethyl aminomalonate **5**[11,12] in refluxing acetic acid to give dihydronaphtho[1,2-c]pyrrole **6** in excellent yield (Scheme 1). Cleavage of the ethyl ester with sodium hydroxide in refluxing ethylene glycol, followed by formylation with trimethyl orthoformate-TFA, afforded the related aldehyde **7**. Formylpyrrole **7** was found to be a suitable precursor for the synthesis of porphyrins with two adjacent naphtho units (Scheme 2).

SCHEME 2



Condensation of two equivalents of **7** with dipyrrylmethanes **8a** and **8b** in the presence of hydrobromic acid gave the corresponding a,c-biladienes **9** in 73-93% yield (Scheme 2). Cyclization with copper(II) chloride in DMF,[13] followed by demetallation with 15% sulfuric acid-TFA, gave the novel porphyrins **10** in good overall yields. Porphyrin **10a** proved to be highly insoluble in common organic solvents and was not further studied. However, **10b** was reasonably soluble and could easily be dehydrogenated with two equivalents of DDQ in refluxing toluene to give the corresponding dinaphthoporphyrin **11**. ^1H NMR ($TFA-CDCl_3$): δ -2.74 4H, br, 4 x NH), 3.15 (4H, t, 2 x CH_2CO), 3.72 (6H, s), 3.75 (6H, s) (2 x porphyrin-CH_3 and 2 x OCH_3), 4.53 (4H, t, 2 x porphyrin-CH_2), 8.13 (2H, t), 8.38 (2H, t), 8.59 (2H, d), 8.93 (2H, d), 9.68 (2H, d), 9.99 (2H, d) (12 x naphthalene-H), 10.93 (1H, s), 11.53 (2H, s), 11.55 (1H, s) (4 x *meso*-H).

SCHEME 3



Porphyrins bearing two fused naphthalenes on the opposite pyrrole rings were also targeted for synthesis (Scheme 3). Dihydronaphtho[1,2-c]pyrrole **6** was transesterified with benzyl alcohol containing catalytic sodium benzyloxide to give the corresponding benzyl ester **12** (Scheme 3). Reaction with lead tetraacetate in acetic acid afforded the corresponding acetoxymethylpyrrole **13**. Acetate **13** condensed with α-unsubstituted pyrroles **14**[14] in the presence of Montmorillonite clay[15] to give the dipyrrylmethanes **15** in good yields. Cleavage of the *tert*-butyl esters with TFA and formylation with trimethyl orthoformate-TFA gave the monoaldehydes **16** in 55-67% yield. Hydrogenolysis of the benzyl esters with H_2 over 10% palladium-charcoal afforded the corresponding carboxylic acids **17** and subsequent "head-to-tail" self-condensation under modified MacDonald conditions[16] gave the centrosymmetric porphyrins **18** in good yields. In common with porphyrin **10a**, **18a** and **18b** were very insoluble in organic solvents. The presence of propionate sidechains again increased the solubility of these porphyrins and **18c** could be handled reasonably easily. Oxidation of **18c**, again using two equivalents of DDQ in refluxing toluene, was particularly facile and gave the oppositely substituted dinaphthoporphyrin **19** in virtually quantitative yield (Scheme 3). ^{1}H NMR (TFA-$CDCl_3$): δ -2.35 (2H, br), -2.15 (2H, br) (4 x NH), 3.24 (4H, t, 2 x CH_2CO), 3.74 (6H, s), 3.76 (6H, s) (2 x porphyrin-CH_3 and 2 x OCH_3), 4.53 (4H, t, 2 x porphyrin-CH_2), 8.09 (2H, t), 8.35 (2H, t), 8.57 (2H, d), 8.89 (2H, d), 9.69 (2H, d), 9.94 (2H, d) (12 x naphthalene-H), 11.24 (2H, s), 11.49 (2H, s) (4 x *meso*-H).

The electronic spectra of porphyrins **11** and **19** in CH_2Cl_2 are quite distinctive (Fig. 1) and showed the anticipated bathochromic shifts to the Soret and Q absorption bands[17] compared to naphthoporphyrin **3**. Band I was shifted to 644 nm in **11** and 641 nm in **19**, although the intensity was somewhat higher in the former porphyrin. Band III undergoes a significant hyperchromic shift in both spectra, and is particularly dominant for the oppositely substituted dinaphthoporphyrin **19**. Ongoing investigations are being directed towards the synthesis of porphyrins fused to larger polycyclic aromatic units and these studies should allow more a detailed interpretation of these unusual electronic spectra.

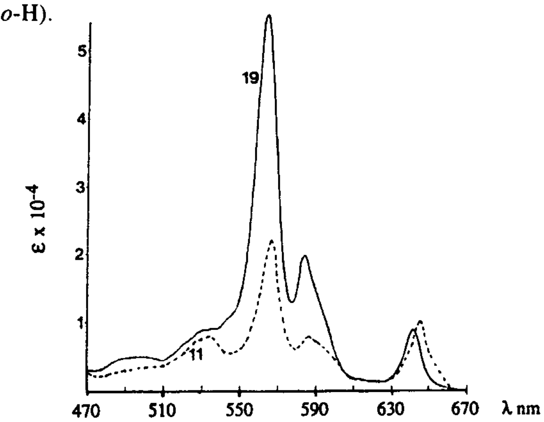


Figure 1: Visible or Q band region of the electronic spectra for dinaphthoporphyrins **11** and **19** in dichloromethane. The Soret bands for **11** and **19** are omitted and appear at 424 and 425 nm, respectively.

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17. Porphyrins are classically considered to have four Q bands, labelled from high to low wavelength as bands I-IV.

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