An improved synthesis of tetraarylporphyrins

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Abstract. An improved synthesis for 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin, 5,10,15,20-tetrakis(2,4,6-trimethylphenyl)porphyrin and 5,10,15,20-tetrakis(2,6-dichlorophenyl)porphyrin by an acid-catalysed condensation of pyrrole and properly substituted aldehyde, followed by oxidation, is reported, with yields of up to 30% being obtained.

Recent results in biomimetic epoxidation reactions, using sodium hypochlorite as “single-oxygen donor” and catalysed by manganese(III) tetraarylporphyrins, have established that this system provides a valuable epoxidation method1,2 (eq. 1).

\[ \text{Mn}^{11+} + \text{OCl}^- \rightarrow \text{Mn}^{11+} = \text{O} + \text{Cl}^- \] (1)

\[ \text{Mn}^{11+} = \text{O} + \text{alkene} \rightarrow \text{Mn}^{11+} + \text{epoxide} \]

Until now, the major drawback of this system has been the low yield of porphyrin catalysts. Simple derivatives, such as 5,10,15,20-tetraphenylporphyrin (TPP), are quickly produced in yields of up to 40% by condensing pyrrole and (substituted) benzaldehyde in refluxing propionic acid3. The widely applied 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin (TPFPP) is prepared in a similar manner in only 10% yield4. To prevent dimerization (eq. 2) and catalyst loss, which are both caused by a bimolecular destruction reaction5, a sterically hindered catalyst, e.g. 5,10,15,20-tetrakis(2,4,6-trimethylphenyl)porphyrin (TMP) or 5,10,15,20-tetrakis(2,6-dichlorophenyl)porphyrin (TDCIPP), can be employed.

\[ \text{Mn}^{11+} = \text{O} + \text{Mn}^{11+} \rightarrow \text{Mn}^{11+} = \text{O} = \text{Mn}^{11+} \] (2)

\[ \text{Mn}^{11+} = \text{O} + \text{Mn}^{11+} \rightarrow \cdots \rightarrow \text{destruction} \]

In general, this class of porphyrins is obtained from the reaction of pyrrole with properly substituted benzaldehyde in pyridine or collidine at 170–180 °C for two days in the presence of zinc acetate. Yields, however, rarely exceed 5% and the work-up is tedious6,7.

Here, we describe a simple procedure for obtaining sterically hindered porphyrins, as well as the pentafluoro derivative, in higher yields. The procedure is based on the strategy developed by Lindsey8, in which, in an acid-catalysed reaction, cyclization of pyrrole and aldehyde to porphyrinogen (eq. 3) is favoured over linear polymerization [poly(pyrrolmethane) formation]. Once equilibration is complete, the porphyrinogen is oxidised by para-chloranil (PCA) or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). In the original article, it was noted that sterically hindered aldehydes gave low yields of porphyrin. Using a modified procedure involving a larger amount of catalyst and extended reaction times, we were able to prepare TMP, TDCIPP and TPFPP in improved yields9,10. As a catalyst, BF3·etherate gives better results than does trifluoroacetic acid and PCA is superior to DDQ in the oxidation step. The work-up procedure includes a simple flash-chromatographic separation or a Soxhlet extraction.

Experimental

A 1-dm3 three-necked, round-bottomed reaction vessel, wrapped in aluminium foil and equipped with a reflux condenser and N2 inlet, was charged with 400 cm3 of CH2Cl2 (distilled from CaCl2),
50 cm$^3$ of 0.10 M pyrrole in CH$_2$Cl$_2$ and 50 cm$^3$ of 0.10 M aldehyde in CH$_2$Cl$_2$. The mixture was stirred and purged with N$_2$ for 10 min, after which 0.2 cm$^3$ of a 0.5 M BF$_3$-etherate solution in CH$_2$Cl$_2$ was added. The solution rapidly turned orange. Subsequently, the mixture was stirred for 20 h at room temperature. PCA (0.922 g, 3.7 mmol) was then added to the red solution. After refluxing for 1 h, the dark purple solution was concentrated to 100 cm$^3$ and 10 g of neutral alumina is added, whereafter all solvent was removed. TDCIPP. The porphyrin adsorbed on alumina was placed in a Soxhlet apparatus and impurities extracted for 24 h with methanol. Subsequently, the porphyrin was extracted with CHC$l_3$. After having been concentrated, the porphyrin was further purified by flash chromatography over neutral alumina (5 x 10 cm, CHC$l_3$). The porphyrin was collected at the first purple band. Yield 334 mg (30%) of purple powder. 'H NMR (CDCl$_3$, 200 MHz) $\delta$: 8.61 (s, 8H, P-pyrrole), 7.72 (t+s, 12H, phenyl), 2.59 (broad s, 2H, NH). UV/Vis (CHC$l_3$, in nm (log e)): 418 (Soret, 3.54), 514 (4.38), 590 (3.97).

TMP. The porphyrin adsorbed on alumina was placed on a column (neutral alumina, 15 x 3 cm) and eluted with CHC$l_3$. Yield 284 mg (29%) of purple powder. 'H NMR (CDCl$_3$, 200 MHz) $\delta$: 8.62 (s, 8H, P-pyrrole), 7.26 (s, 8H, m-phenyl), 2.62 (s, 12H, p-methyl), 1.85 (s, 24H, o-methyl), 2.51 (broad s, 2H, NH). UV/Vis (CHC$l_3$, in nm (log e)): 418 (Soret, 5.61), 515 (4.29), 548 (3.92), 592 (3.85), 646 (3.62).

TPFPP. Procedure similar to that of TMP except for the eluent CHCl$_3$/hexane 7:3 (v/v). Yield 329 mg (27%) of purple powder. 'H NMR (CDCl$_3$, 200 MHz) $\delta$: 8.8 (s, 8H, P-pyrrole), 7.26 (s, 8H, m-phenyl), 2.50 (broad s, 2H, NH). UV/Vis (CHC$l_3$, in nm (log e)): 411 (Soret, 5.42), 507 (4.37), 584 (3.99), 658 (3.79). The procedure may be adapted to yield gram quantities of porphyrin. For the sake of convenience, i.e. less optimised conditions, were employed resulting in slightly lower yields. The preparation of TMP may serve as an example. A 3-dm$^3$ reaction vessel wrapped in aluminium foil was charged with 2 dm$^3$ of dry CH$_2$Cl$_2$, 2.68 g of pyrrole (0.04 mol) and 5.93 g of mesityl aldehyde (0.04 mol). After purging with N$_2$ for 10 min, 2 cm$^3$ of a 0.5 M BF$_3$-etherate solution in CH$_2$Cl$_2$ was added. After stirring at room temperature under N$_2$ for 20 h, 7.38 g of PCA (0.03 mol) was added. The mixture was refluxed for 1 h and worked up in the usual way. Yield 2.0 g of TMP (26%). NMR and UV/Vis as given above.

References
10 While this work was in progress, a paper appeared describing an improved synthesis of TMP using the Lindsey procedure: R. W. Wagner, D. S. Lawrence and J. S. Lindsey, Tetrahedron Lett. 28, 3069 (1987). This procedure gives a good yield but is not suitable for gram-scale preparations from a practical point of view, since high dilution conditions are employed (e.g. 563 mg require 1 dm$^3$ of solvent).
11 We were unsuccessful in preparing 5,10,15,20-tetrakis(9-anthryl)porphyrin and 5,10,15,20-tetrakis[(2,4,6-triphenyl)phenyl]porphyrin by this method.