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SYNTHESIS OF TETRAPHENYLPORPHYRINS UNDER VERY MILD CONDITIONS

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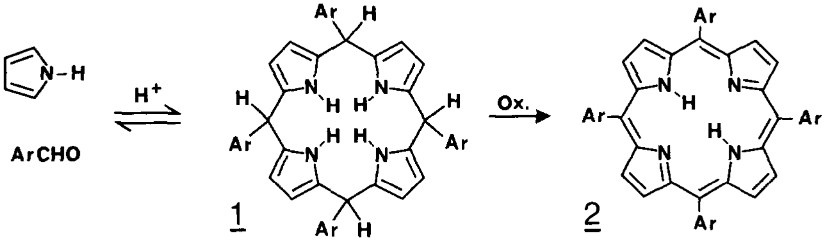
Abstract: Reaction of pyrrole and an aromatic aldehyde at room temperature affords the corresponding tetraarylporphyrinogen in high yield at thermodynamic equilibrium. Oxidation yields the porphyrin. The reaction conditions are of broad scope.

Tetraphenylporphyrins have been widely exploited in the development of porphyrin model systems. The synthesis of tetraphenylporphyrin developed by Adler involves the addition of benzaldehyde and pyrrole to an open bath of refluxing propionic acid.[1] Though the Adler reaction affords yields of 20% with simple benzaldehydes and can be performed on a large scale, it also suffers from several limitations. First, the reaction fails completely with benzaldehydes bearing sensitive functional groups. Second, intractable purification problems arise for porphyrins which do not readily crystallize or precipitate from the tar-laden propionic acid. Third, the yields obtained are often not reproducible.

We sought to develop an alternative procedure, complementary to that of Adler, which would allow small quantities of porphyrins to be cleanly prepared from sensitive aldehydes in high yield. In pursuit of reaction conditions sufficiently gentle to meet these requirements, several chemical precedents concerning the thermodynamic stability of macrocyclic structures suggested the following synthetic strategy:[2] *Choose reaction conditions which allow condensation of pyrrole and the benzaldehyde to reach equilibrium, where the cyclic tetraarylporphyrinogen is thermodynamically favored over the linear polypyrrylmethanes. An oxidant can then be added to irreversibly convert the porphyrinogen to the porphyrin. Reaction conditions sufficiently mild for equilibrium to be attained will likely also be compatible with a wide variety of functional groups.* The viability of this strategy is largely borne out by the data we now present.

Pyrrole and the desired benzaldehyde (10^{-2} M) are allowed to react at room temperature in dry CH_2Cl_2 under N_2 with trace acid catalysis (10^{-3} M BF_3 or 10^{-2} M trifluoroacetic acid). The reaction is reversible under these conditions and the system reaches equilibrium in about 1 h. A stoichiometric amount of p-chloranil (39° C, 1 h) is then added to irreversibly oxidize the tetraarylporphyrinogen 1 to the porphyrin 2 and the polypyrrylmethanes to polypyrrylmethenes. The general product work-up involves concentration of the crude reaction mixture followed by passage over a short chromatography column. The polypyrrylmethenes exhibit no properties characteristic of tars and usually bind at the top of the column. The porphyrin product obtained in this manner is relatively pure.

The yield at equilibrium is critically dependent on the reactant concentrations. With benzaldehyde and pyrrole at 10^{-2} M, the porphyrin yield is 46%.[3] The yield falls markedly at both higher (10^{-1} M, 14%) and lower (10^{-3} M, 16%) concentrations. Equilibrium mass action considerations suggest that the higher yield at 10^{-2} M results from a balance between the competing cyclization and polymerization processes.[4]



The procedure is mild, clean, and convenient. Quantities of porphyrins up to 1 gm, enough for most research applications, are readily prepared. Now for the first time new classes of substituted benzaldehydes have been converted to the porphyrin in 30-40% yield. These include but are not restricted to benzaldehydes bearing phenacyl and alkyl esters, benzyl and alkyl ethers, alcohols, dithiolanes, acetals from 2,2-dimethylpropanediol, and other multiple functionalities.[5] This equilibrium strategy should open new vistas in preparing increasingly sophisticated porphyrin model systems.

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2. J. S. Lindsey, D. C. Mauzerall, J. Am. Chem. Soc. 104 (1982) 4498. D. Mauzerall, J. Am. Chem. Soc. 82 (1960) 2601, 2605. B. Franck, Angew. Chem. Int. Ed. Engl. 21 (1982) 343.

3. Yields of 50-60% are obtained when 1 equiv (10^{-2} M) of triethylorthoacetate is included as a water scavenger (with BF_3 catalysis only).

4. H. Jacobson, W. H. Stockmayer, J. Chem. Phys. 18 (1950) 1600.

5. Each porphyrin prepared from phenacyl 4-formylbenzoate, phenacyl 3-formylbenzoate, butyl-4-formylbenzoate, 4-benzyloxybenzaldehyde, p-octyloxybenzaldehyde, 4-(2-hydroxyethoxy)-benzaldehyde, 2-(4-formylphenyl)-1,3-dithiolane, 2-(3-formylphenyl)-1,3-dithiolane, and 2-(4-formylphenyl)-5,5-dimethyl-1,3-dioxane has been characterized by UV-VIS, IR, and NMR spectroscopy, and fission fragment mass spectrometry.

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