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Porphyrin Synthesis Using Clays. Taking Advantage of Statistical Product Distributions

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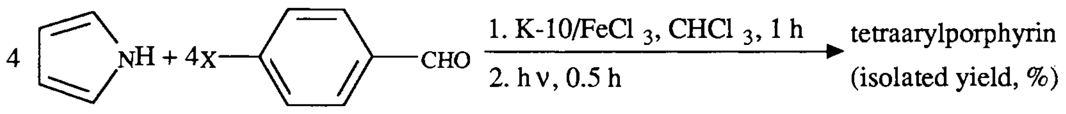
Solid acids such as the K10 montmorillonite are useful for preparation of porphyrins from pyrrole condensed with aldehydes. Combining the use of two different aldehydes A and B with unequal, statistical proportions of A and B allows maximization of the relative amount of the desired mixed porphyrin.

Publication by Onaka *et al.*1) of an improved synthesis of *meso*-tetraalkylporphyrins spurs us to report closely related work. The handsome results by the Nagoya group were achieved by recourse to the K10 montmorillonite clay2) as a solid acid. As a consequence of this work,1) both *meso*-tetraalkyl- and *meso*-tetraphenylporphyrins3,4) can now be made in the presence of montmorillonites as catalysts from pyrrole and the appropriate RCHO or ArCHO aldehyde. However, this provides only porphyrins of the R_4 or Ar_4 type, in which the four R(Ar) substituents are all the same. We show here a useful generalization: by choosing carefully the relative amounts of the reactants, it is possible to make such synthesis highly selective for the desired porphyrin. General principles are: consider a synthesis in which - most likely in a stepwise manner - four fragments are combined. Suppose furthermore that there are only two kinds of component parts, labeled A and B. With equal concentrations of A and B, and in the absence of discrimination, i.e. if attachement of A and B are equiprobable processes then five distinct products A_4, A_3B, A_2B_2, AB_3, and B_4 arise. Their relative amounts obey the very simple binomial distribution 1:4:6:4:1. It is an easy matter to calculate the other binomial distributions arising from *unequal* initial concentrations of A and B. Let us now assume that A_3B is the target molecule. If the synthesis leads to a statistical distribution of products, one will maximize the relative amount of A_3B by setting up the reactants so that A be in excess of B. Examination of Table 1 shows that calculations bear out the intuition: the relative abundance of A_3B should be maximum at a reactant ratio of 3 A's to 1B.

Table 1. Calculated Relative Percentages of the Various Products Resulting From Assembly of Four Fragments A and B, in a Purely Statistical Manner

	A_4	A_3B	A_2B_2	AB_3	B_4
1A + 1B	6.35	25.00	37.50	25.00	6.35
2A + 1B	19.75	39.51	29.63	9.87	1.23
4A + 1B	40.96	40.96	15.36	2.56	traces

Experimental confirmation is that porphyrins have been obtained from pyrrole condensed with aldehydes using clays. We observed formation of tetraphenylporphyrin to be catalyzed by various Lewis acids[1,3-9] ($FeCl_3$, $ZnCl_2$, $AlCl_3$, $SbCl_5$) in the initial condensation steps. We opted for an $FeCl_3$-doped K10 montmorillonite. The method works nicely, under mild conditions. Control experiments showed that the clay enhances Lewis acid catalysis, plausibly because the reduced dimensionality of the reaction space makes for more frequent diffusional encounters between the reactants. Competing formation of oligomers and polymers is responsible for the relatively low yields, which we made no attempt to optimize since selectivity, not yield, was our main objective. We then performed a condensation from mixed starting materials, *viz.* benzaldehyde (X=H) and p-anisaldehyde ($X=OCH_3$), using identical reaction conditions. The results were quite gratifying, we obtained in 22% overall yield the mixture of the tetraarylporphyrins **1-6**. Thus, the above difference in yields, 20% and 10% respectively, does not appear to effect a substantial difference in the intrinsic reactivities.



X	
X = H	20.0
CH_3	18.2
OCH_3	10
Cl	9.1
NO_2	1.5
CN	1.5

1 $Ar_1 = Ar_2 = Ar_3 = Ar_4 = C_6H_5$

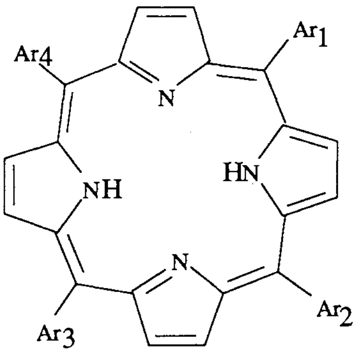
2 $Ar_1 = p\text{-}CH_3OC_6H_4$; $Ar_2 = Ar_3 = Ar_4 = C_6H_5$

3 $Ar_1 = Ar_2 = p\text{-}CH_3OC_6H_4$; $Ar_3 = Ar_4 = C_6H_5$

4 $Ar_1 = Ar_3 = p\text{-}CH_3OC_6H_4$; $Ar_2 = Ar_4 = C_6H_5$

5 $Ar_1 = Ar_2 = Ar_3 = p\text{-}CH_3OC_6H_4$; $Ar_4 = C_6H_5$

6 $Ar_1 = Ar_2 = Ar_3 = Ar_4 = p\text{-}CH_3OC_6H_4$



Using equimolar amounts of the two aldehydes, one gets a statistical distribution of all the expected products (Table 2).

Table 2. Porphyrin Preparation From Equimolar Ratio of Benzaldehyde and p-Anisaldehyde Condensed With Pyrrole

Product	1	2	(3 + 4)	5	6
% obsd, ± 2%	5	25	41	31	6
% calcd	6.35	25.4	38.1	24.4	6.35

These reaction products may be analyzed by HPLC (RP-18, CH_3CN-THF = 95-5). Preparative scale separation is performed by column chromatography (SiO_2, $CHCl_3$). Each isomer is characterized easily, on account of its symmetry, from its ^1H and ^{13}C nmr spectra. Since mixed porphyrins of the types **2-5** are anyhow of difficult access, the present statistical method, because of its acceptable yield, and the mild reaction conditions, compares favorably with existing methods.[10-22] Furthermore, the methodology is easily biassed towards predominant formation of one of the products at will. These were our results, to be compared with the calculated distributions in Table 1 (Table 3).

Table 3. Porphyrin Preparation From Non-Equimolar Ratios of Benzaldehyde and p-Anisaldehyde Condensed With Pyrrole

Product	**1**	**2**	**3 + 4**	**5**	**6**
Reactant ratio = 1:2	1	9	30	39	21
2:1	16	40	35	9	traces
4:1	33	45	20	3	traces

4 mmol of $FeCl_3$ and 4 g of K10 are ground together. The resulting yellow powder (5.3 g) (caution: do not inhale) is used immediately. To 4 mmol of the aromatic aldehyde dissolved in 50 mL of chloroform add 1.3 g of the solid acid and stir at room temperature for 1 h. After filtering off the suspended clay particles, illuminate the solution for 30 mn in the visible with a 1250 W lamp (TOS 1250), or for 2 d under normal sunlight. The individual reaction products are obtained, after solvent elimination and column chomatography on silicagel (one to eliminate residual polymers, and another to effect the separation).

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