C, 68.20; H, 3.85; N, 10.90. Calcd: C, 68.56; H, 3.92; N, 10.91.

16h. After **10h** was heated for 18 h with PPSE/$MeNO_2$, the mixture was poured into water, and the solid formed was collected by filtration and dried. The solid, diglyme (10 mL), and a catalytic amount of Pd-C (10%) were heated at reflux for 20 h. The mixture was allowed to cool, filtered, and poured into water. The precipitate formed was collected by filtration and dried (200 °C, 0.05 mbar) to give **16h** (0.22 g, 61%) as a red-brown solid: ^1H NMR (200 MHz, DMSO-d_6) δ 11.85 (2 H, s), 11.09 (1 H, s), 8.66 (2 H, dd), 7.9-7.8 (2 H, m), and 7.5-7.4 (2 H, m); MS 361 (M^+, 100), 290 (26), 180 (13), 145 (19).

Repetition of this experiment (10-mmol scale) gave the product in 80% yield after recrystallization from DMF.

16i. After **10i** was heated for 16 h with PPSE/$MeNO_2$, the mixture was poured into water, and the solid formed was collected by filtration and dried. the solid, diglyme (10 mL), and a catalytic amount of Pd-C (10%) were heated at reflux for 20 h. The mixture was filtered hot and allowed to cool. The precipitate formed was collected by filtration and dried (200 °C, 0.05 mbar) to give **16i** (0.18 g) as an orange crystalline solid: mp >360 °C. The analytical sample was recrystallized from DMF. Found: C, 61.20; H, 2.34; N, 10.37; Cl, 18.08. Calcd: C, 60.93; H, 2.28; N, 10.66; Cl, 17.99. A second crop (0.11 g) was obtained by pouring the filtrate into water and collecting the solid that formed: total yield 74%; ^1H NMR (200 MHz, DMSO-d_6) δ 11.98 (2 H, s), 11.16 (1 H, s), 8.98 (2 H, s), 7.88 (2 H, d), and 7.59 (2 H, m). MS 393 (M^+, 100), 358 (19), 323 (12), 287 (8). Peaks containing ^{37}Cl are not listed.

16j. After **10j** was heated for 20 h with PPSE/$MeNO_2$, the mixture was poured into water, and the solid formed was collected by filtration and dried. The solid was washed several times with hot EtOAc and dried (200 °C, 0.05 mbar) to give **16j** (0.36 g, 78%) as an golden-yellow solid: mp >360 °C; ^1H NMR (200 MHz, DMSO-d_6) δ 11.94 (2 H, s), 11.14 (1 H, s), 9.10 (2 H, s), 7.81 (2 H, d), and 6.68 (2 H, d).

Indolization of 10l. After **10l** was heated for 43 h with PPSE/$MeNO_2$, the mixture was poured into water, and the solid formed was collected by filtration and dried to give an orange solid (0.47 g). ^1H NMR analysis revealed a mixture of isomers.

1-Chloroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7(6*H*)-dione (16m). After **10m** (64 mg, 0.13 mmol) was heated for 2 h with PPSE/$MeNO_2$, the mixture was poured into water and extracted twice with EtOAc. The combined extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to give an orange oil, which was refluxed with Pd-C (catalyst) and diglyme (2 mL) for 8 h, allowed to cool, filtered, and poured into water. The mixture was extracted twice with EtOAc. The combined extracts were washed with water and brine, dried ($MgSO_4$), and concentrated to give an orange material, which was triturated with acetone to give **16m** (14 mg, 24%) as an orange solid, mp >360 °C.

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Registry No. **4a**, 118458-54-1; **6**, 31411-71-9; **7a**, 1631-26-1; **7** (R = H), 541-59-3; **8a**, 118458-37-0; **8b**, 118458-36-9; **9a**, 100-63-0; **9c**, 18312-46-4; **9d**, 10449-07-7; **9e**, 15384-39-1; **9f**, 40887-80-7; **9g**, 3471-32-7; **9h**, 371-14-2; **9i**, 1073-69-4; **9j**, 589-21-9; **9k**, 100-16-3; **9l**, 13123-92-7; **10a**, 118458-38-1; **10b**, 118458-40-5; **10c**, 118458-41-6; **10d**, 118458-42-7; **10e**, 118458-43-8; **10f**, 118458-44-9; **10g**, 118458-45-0; **10h**, 118458-46-1; **10i**, 118458-47-2; **10j**, 118458-48-3; **10k**, 118458-49-4; **10l**, 118458-50-7; **10m**, 118458-51-8; **11**, 118458-39-2; **15a**, 118458-52-9; **15b**, 118458-53-0; **16a**, 87259-91-4; **16c**, 118458-55-2; **16d**, 118458-56-3; **16e**, 118458-57-4; **16g**, 118458-58-5; **16h**, 118458-59-6; **16i**, 118458-60-9; **16j**, 118458-61-0; **16m**, 118458-62-1.

Investigation of the Synthesis of Ortho-Substituted Tetraphenylporphyrins

Jonathan S. Lindsey* and Richard W. Wagner

Department of Chemistry, Carnegie Mellon University, 4400 Fifth Avenue, Pittsburgh, Pennsylvania 15213

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Ortho-disubstituted tetraphenylporphyrins such as tetramesitylporphyrin have been widely used in model systems, but these "sterically hindered" porphyrins have been difficult to synthesize under mild as well as forcing conditions. Mesitaldehyde is highly discriminating in its exacting requirements for catalysis, but little steric hindrance is observed when these catalytic requirements are satisfied. A key feature of these catalytic conditions involves BF_3-ethanol cocatalysis. Application of these conditions to 14 ortho-substituted benzaldehydes resulted in a clear reactivity pattern: cocatalysis gave improved yields with 2-alkyl-, 2-alkoxy-, and 2,6-dialkoxybenzaldehydes, but six *o*-halogen-substituted benzaldehydes showed little or no increase. Four ortho-disubstituted aldehydes failed to react under any conditions. The structural effects of substituents can be partly understood by examining the packing of the aldehyde ortho substituents about the tetrahedral meso carbon in the porphyrinogen, the precursor to the porphyrin.

Introduction

Few classes of synthetic porphyrins have aroused more interest yet remained more difficult to prepare than the sterically hindered porphyrins.[1] Tetramesitylporphyrin, the test case for gauging the success of new methods for preparing sterically hindered porphyrins, has been prepared in yields of 1-6% by reaction of mesitaldehyde and pyrrole at >170 °C for 2-3 days in the presence of added metal salts.[2-6] That forcing conditions might be required to overcome steric hindrance with mesitaldehyde is hardly surprising; the concept of steric hindrance was first pos-

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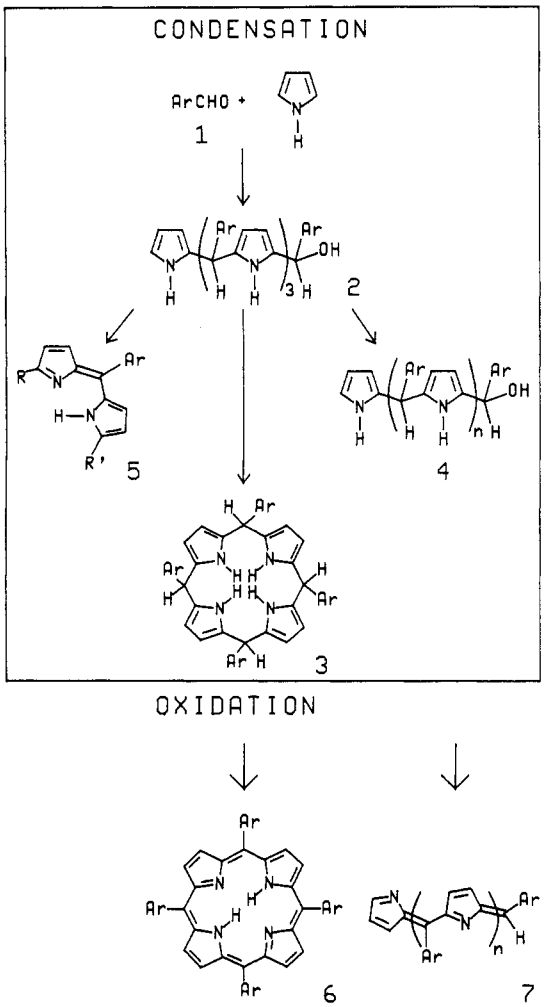
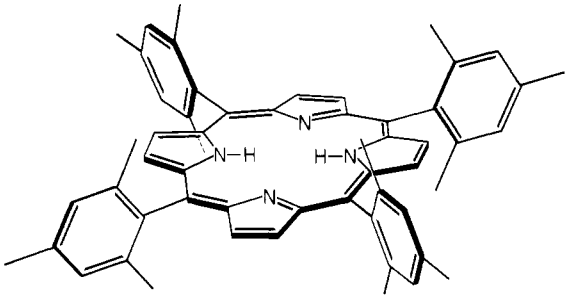


Figure 1. Schematic outline of porphyrin formation. Condensation of an aldehyde (1) and pyrrole gives the tetrapyrromethane (2) which can cyclize to the porphyrinogen (3) or continue polymerization to give higher molecular weight polypyrromethanes (4). Formation of dipyrrins (dipyrromethenes) (5) can occur at any site in the polypyrromethane chain. The addition of an oxidant converts the porphyrinogen to the porphyrin (6) and the polypyrromethanes to polypyrromethenes (7). The hypothetical structure 7 represents the polypyrromethenes in their maximally dehydrogenated form; the extent of dehydrogenation is not known.

tulated (ca. 1894) as a result of studies in the mesityl family.[7]



tetramesitylporphyrin

We recently developed a method for preparing porphyrins under gentle conditions at room temperature. Pyrrole and aldehyde undergo acid-catalyzed condensation to form a porphyrinogen, which is converted to the porphyrin in a second step upon addition of an oxidant

(7) *Steric Effects in Organic Chemistry*; Newman, M. S., Ed.; John Wiley and Sons, Inc.: New York, 1956; pp 201–248.

Table I. Product Distribution in Mesitaldehyde Condensations: Effect of Acid and Temperature[a]

		yield, %		
acid catalyst[b]	temp, °C	mesitaldehyde	dipyrrins	TMP
BF_3	25	5	5	31
BF_3	61	≤1[c]	20	20
TFA	25	100	0[d]	0
TFA	61	100	0[d]	0
BCl_3	25	8	51	0
BCl_3	61	15	46	0

[a] The reactions were performed in $CHCl_3$. The yields were determined after 1 h of reaction. The yield of unreacted mesitaldehyde was determined by TLC (silica, CH_2Cl_2). Dipyrrin formation was monitored spectroscopically at 480 nm (assuming ϵ = 60 000 M^{-1} cm^{-1}). Porphyrin yields were determined by oxidizing an aliquot from the reaction vessel with excess DDQ at room temperature, followed by absorption spectrophotometry. [b] Concentrations of BF_3·OEt_2, trifluoroacetic acid (TFA), and BCl_3 were each 3.3 mM. [c] Below the limits of detection on TLC. [d] The reaction turned yellow upon addition of TFA, but no dipyrrins (<0.1%) were detected.

(Figure 1).[8] The reaction conditions optimized for benzaldehyde, however, failed to support the reaction of mesitaldehyde.[8] In seeking to understand the mechanistic origins of the unreactivity of mesitaldehyde in the two-step reaction process, we found that tetramesitylporphyrin was formed in 30% yield under slightly modified reaction conditions.[9] In this paper we show that the modified reaction conditions involve BF_3–ethanol cocatalysis. We describe the sensitivity of the formation of tetramesitylporphyrin to the solvent, temperature, catalyst, cocatalyst, and concentrations of reactants and catalysts. The scope of these conditions is defined by the successful reaction of 14 out of 18 ortho-substituted aryl aldehydes. Finally, porphyrin yield data from this survey are used to develop a model of the structural effects of ortho substituents in porphyrin formation.

Results

Reaction Optimization. Tetramesitylporphyrin (TMP) formation was studied in the context of the two-stage reaction shown in Figure 1. In an attempt to distinguish between and overcome possible steric barriers to condensation or oxidation, we first performed the condensation and oxidation at different temperatures. The condensation of mesitaldehyde and pyrrole was performed in CH_2Cl_2 by using conditions (25 °C, reactants 10^{-2} M each, BF_3 10^{-3} M) optimized for tetraphenylporphyrin (TPP). Aliquots were removed and subjected to oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in refluxing toluene (110 °C), but no TMP was formed, even with increased acid concentrations and longer condensation and oxidation times. The condensation was then attempted in several solvents with higher boiling points than that of CH_2Cl_2 (39 °C), including *o*-dichlorobenzene (179 °C) and $CHCl_3$ (61 °C). No TMP was obtained in *o*-dichlorobenzene over a range of temperatures, but TMP formed readily in refluxing $CHCl_3$. The yield reached 14% when both the condensation and oxidation were performed at room temperature in $CHCl_3$, proving that high temperatures were not necessary to overcome steric barriers to condensation or oxidation.

In order to fine-tune the catalytic conditions, the concentrations of acid catalyst and reactants were systemat-

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(9) Wagner, R. W.; Lawrence, D. S.; Lindsey, J. S. *Tetrahedron Lett.* **1987**, *28*, 3069–3070.

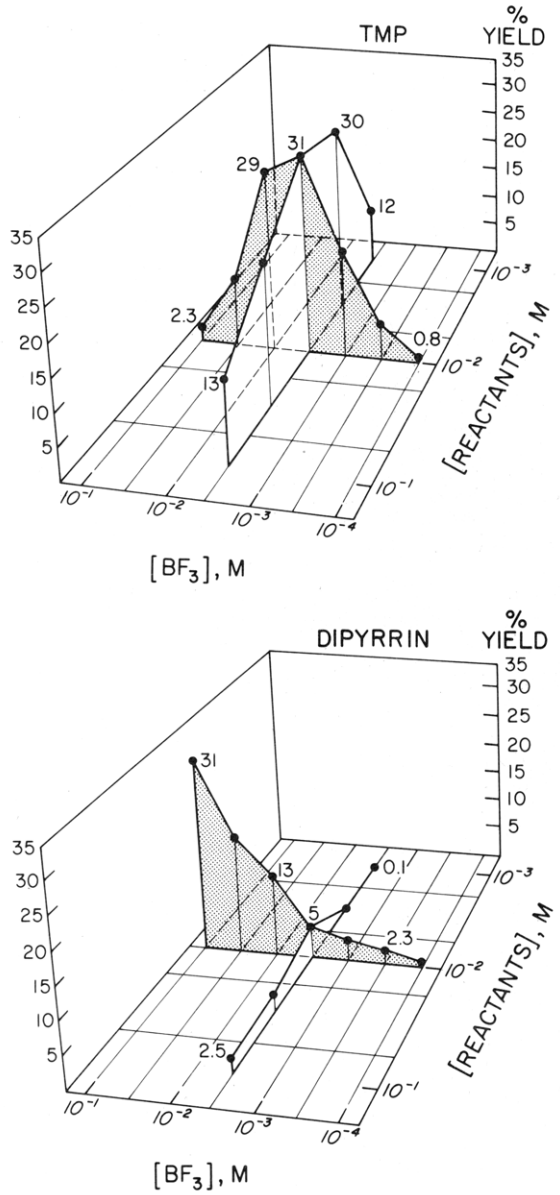


Figure 2. Tetramesitylporphyrin formation: dependence on concentrations of reactants and acid catalyst. The decline in yield of TMP (upper graph) with high acid concentrations is accompanied by increased yields of dipyrrins (lower graph). The condensations were performed at room temperature, and the porphyrin yields were determined spectrophotometrically after oxidation of reaction aliquots at room temperature with excess DDQ. The reactions were sampled at 15-min intervals, and the porphyrin yields generally had plateaued at 45–60 min. The porphyrin yields shown are the highest obtained during a 1-h condensation. The dipyrrin yields were determined after 1 h of reaction.

ically varied in the room temperature condensation in $CHCl_3$. Increasing the acid concentration to 3.3 mM BF_3 resulted in a 31% yield of porphyrin after 1 h of reaction (Figure 2). Subsequently changing the pyrrole and mesitaldehyde concentrations from 10^{-2} M (equimolar) with fixed BF_3 concentration (3.3 mM) resulted in lowered yields (Figure 2).

The effect of temperature was examined by performing the condensations at 25 and 61 °C in $CHCl_3$ using these improved catalytic conditions (Table I). In contrast to the 31% yield at room temperature, the yield of porphyrin in refluxing $CHCl_3$ was only 20%. The reaction was faster in refluxing $CHCl_3$, but at no point during the condensation did the porphyrin yield exceed 20%. The yield of dipyrrins (**5**, Figure 1) after 1 h was greater in refluxing $CHCl_3$ (20%) than at room temperature (5%). The effect of increased temperature is to shunt the starting materials to dipyrrins rather than to increase the yield of porphyrin.

Table II. Solvent Dependence and Ethanol Cocatalysis in TMP Formation[a]

solvent	additive,[c] %	yield, % TMP	yield, % dipyrrins
$CHCl_3$[b]	EtOH: 0	0[d]	0.4
	0.1	25	13[e]
	0.75	30	14[e]
	2.0	20	15[e]
CH_2Cl_2	EtOH: 0	0	1.1
	0.1	23	10
	0.75	25	10
	1.0	19	9.1
	2.0	14	12
	5.0	4	16
	AcOH: 0.75	1.8	5.3
	t-BuOH: 0.75	5.5	1.8
	Et_2O: 1.4	0	0.2
CCl_4	EtOH: 0	2[d]	0.1
	0.75	11	5.9

[a] Yields were determined after 1 h at room temperature; 0.75% ethanol (0.13 M) and 3.3 mM BF_3 corresponds to an ethanol:BF_3 ratio of ~50:1. [b] $CHCl_3$ depleted of ethanol by chemical treatment. [c] Percent vol/vol. [d] Precipitates formed upon adding $BF_3 \cdot OEt_2$, and the reaction mixture turned orange over the course of 1 h. [e] The yields of dipyrrins in ethanol-depleted $CHCl_3$ were higher than those in $CHCl_3$.

The reaction also is quite sensitive to the type of acid catalyst. The catalysts trifluoroacetic acid and BCl_3 readily yield TPP from benzaldehyde and pyrrole, but neither afforded TMP (Table I). With mesitaldehyde and BCl_3, the predominant product was dipyrrins, and with trifluoroacetic acid, little reaction occurred at all and mesitaldehyde could be recovered unchanged. Trifluoromethanesulfonic acid at 10^{-3} M gave results identical with those of TFA, but at 10^{-2} M the reaction mixtures turned orange, precipitates were observed, and dipyrrins formed in 4% yield after 1 h.

Solvent Investigation. The striking reactivity difference of mesitaldehyde in $CHCl_3$ (31% yield) versus CH_2Cl_2 (0% yield) prompted a series of experiments aimed at gaining deeper insight into this solvent effect. One major difference between these similar solvents is that the commercial $CHCl_3$ contained 0.75% (v/v) ethanol as a stabilizer. The addition of 0.75% ethanol to CH_2Cl_2 resulted in a 25% yield of TMP, showing that the solvent effect was due to the presence of ethanol (Table II). Commercial $CHCl_3$ was depleted of ethanol by chemical treatment, and TMP formation failed to occur in absolute $CHCl_3$, just as it did in CH_2Cl_2. Reconstitution by adding 0.75% ethanol to absolute $CHCl_3$ again resulted in ready formation of TMP. The addition of only 0.1% ethanol gave 23% (CH_2Cl_2) and 25% ($CHCl_3$) yields of TMP after 1 h (Table II). The yield of TMP was nearly identical in crude (undistilled) and distilled $CHCl_3$ (from K_2CO_3), indicating that simple distillation was ineffective in removing ethanol from $CHCl_3$. In summary, CH_2Cl_2 and $CHCl_3$ give nearly identical results in the presence of equivalent amounts of added ethanol.

To gain a better understanding of the requirement for added ethanol in the TMP reaction, the IR spectra and BF_3-binding affinities of mesitaldehyde were compared with those of benzaldehyde, which reacts smoothly in the presence or absence of ethanol. The IR spectra in CH_2Cl_2 and $CHCl_3$ showed no solvent dependence in the carbonyl stretching frequencies of mesitaldehyde (1679 cm^{-1}) and benzaldehyde (1704 cm^{-1}), showing that hydrogen bonding with ethanol was not the source of the different reactivity

Table III. Solvent Dependence of Aldehyde–BF_3 Binding[a]

solvent	benzaldehyde–BF_3 K_{assoc}	benzaldehyde–BF_3 $(BF_3)_{1/2}$	mesitaldehyde–BF_3 K_{assoc}	mesitaldehyde–BF_3 $(BF_3)_{1/2}$
CH_2Cl_2	71	400	7100	4[b]
CH_2Cl_2 + EtOH (0.75%)	3.6	8000	8.4	3400
$CHCl_3$	2.9	10000	8.7	3300

[a] The apparent association constant, K_{assoc} (M^{-1}) = $1/[BF_3]_{1/2}$, was determined for 50% bound mesitaldehyde and benzaldehyde by using UV–visible absorption spectroscopy.[10] $(BF_3)_{1/2}$ is the number of equivalents of BF_3 (relative to the aldehyde) added to achieve half-saturation. The aldehyde concentrations were 3.5×10^{-5} M. The spectral properties (λ_{max}, $\epsilon_{\lambda_{max}}$) of the complexes were unchanged in the presence or absence of ethanol. [b] This value was obtained with CH_2Cl_2 distilled from CaH_2 and stored over molecular sieves, 4 Å. Slightly higher values were obtained with less rigorously dried CH_2Cl_2.

Table IV. Acid Catalysis and Ortho-Substituted Aldehydes[a]

aldehyde	porphyrin yield, %: solvent; $[BF_3]$ CH_2Cl_2; 1 mM	CH_2Cl_2 + EtOH (0.75%) 1 mM	CH_2Cl_2 + EtOH (0.75%) 3.3 mM	$CHCl_3$; 3.3 mM
benzaldehyde	30	33	33	49
2-methylbenzaldehyde	35	26	43	50
mesitaldehyde	0	14	25	29
mesitaldehyde (0.1 M)[b]	10[c]		13	

[a] The reactions were performed at room temperature with 10^{-2} M reactants. Yields were determined spectroscopically after oxidizing an aliquot of the reaction mixture with DDQ, using Soret-band extinction coefficients of 500 000 M^{-1} cm^{-1} (tetraphenylporphyrin and tetrakis(2-methylphenyl)porphyrin) and 427 000 M^{-1} cm^{-1} (tetramesitylporphyrin). [b] 10^{-1} M mesitaldehyde and pyrrole. [c] $[BF_3] = 3.3 \times 10^{-2}$ M. Higher or lower BF_3 concentrations gave lower yields (e.g., TMP was formed in 5% yield with 3.3 mM BF_3 and 10^{-1} M reactants), mirroring the yield versus concentration curve obtained in Figure 2.

of benzaldehyde and mesitaldehyde. Next, the binding of BF_3 to the aldehydes was monitored by the red-shifted absorption band in the adducts.[10] The apparent association constant of mesitaldehyde and BF_3 was 100 times greater than that of benzaldehyde and BF_3 in CH_2Cl_2 (Table III).[11] The addition of ethanol displaced the complexes, making approximately equivalent amounts of BF_3 necessary to achieve 50% binding of benzaldehyde and mesitaldehyde. In the presence of ethanol, benzaldehyde and mesitaldehyde showed very similar binding behavior and similar reactivity to form the porphyrin. The poor reactivity of mesitaldehyde in the absence of ethanol results from the unusually stable mesitaldehyde–BF_3 complex.

These observations suggested that TMP formation might be achieved in the absence of ethanol by displacing the mesitaldehyde–BF_3 complex with higher reactant concentrations. When the concentrations of mesitaldehyde and pyrrole were increased 10-fold in CH_2Cl_2 (10^{-1} M each), TMP was formed in 10% yield (Table IV). This yield is comparable to that obtained in $CHCl_3$ (13%, Figure 2) at 10^{-1} M reactants. At these concentrations, 1 g of TMP is obtained from the reaction in 500 mL of solvent.

Synthetic Application. Fourteen ortho-substituted tetraarylporphyrins were prepared by using the reaction conditions found optimal for TMP (Table V). Further variation was explored by performing the condensation and oxidation steps of the reaction in $CHCl_3$ at two different temperatures (25 and 61 °C). The condensations at 25 °C generally leveled off after 45–60 min, but at 61 °C, the porphyrin yields plateaued within 5–15 min. Dipyrrin yields generally increased with temperature, but substantial yields were observed only for mesitaldehyde and 2,4,6-trimethoxybenzaldehyde (Tables I and V).[12] The 14 aldehydes also were reacted in CH_2Cl_2 in order to elucidate the scope of the cocatalysis conditions (Table V). Aldehydes that failed to submit to any conditions include 9-anthraldehyde, 2,4,6-triphenylbenzaldehyde, 2,6-dinitrobenzaldehyde, and 2,6-bis(trifluoromethyl)benzaldehyde. Porphyrins have been prepared successfully via the Adler reaction from 9-anthraldehyde[13] and 2,4,6-triphenylbenzaldehyde[14] in 0.2 and 1% yields, respectively. The reaction of 9-anthraldehyde was studied in the same manner as that of mesitaldehyde. 9-Anthraldehyde reacted with pyrrole, but no porphyrin could be isolated.[15] The reaction of 2,6-bis(trifluoromethyl)benzaldehyde via an improved collidine procedure gives the corresponding porphyrin in 20% yield.[16]

Discussion

The conversion of aldehyde and pyrrole to porphyrin is a multistep process involving condensation (polymerization and cyclization) followed in timed sequence by oxidation. Efficient execution of a one-flask porphyrin reaction requires optimization of numerous reaction parameters. In addition, the intrinsic structure of the reactants must be compatible with each step of the overall process.

(10) Rabinovitz, M.; Grinvald, A. *Tetrahedron Lett.* **1971**, 641–644.

(11) The pK_a of protonated mesitaldehyde (−4.7) is ~2.4 units higher than that of benzaldehyde. See: Yates, K.; Stewart, R. *Can. J. Chem.* **1959**, *37*, 664–671.

(12) The dipyrrins (formerly pyrromethenes or dipyrrylmethenes; for revised nomenclature, see: Moss, G. P. *Pure Appl. Chem.* **1987**, *59*, 779–832) generally absorb in the 470–520-nm region, but this broad peak can encompass a variety of structural types including positional isomers within a chain, tautomers, different protonated forms, tripyrrins and more conjugated polypyrromethenes, and possibly azafulvene components. Furthermore, the measured dipyrrin yield may include dipyrrin moieties in partially oxidized porphyrinogens (5,10,15,20-tetrahydro- and 5,15-dihydroporphyrins). The absorption spectrum provides no distinction between these diverse compounds. To quantitate overall dipyrrin formation we have used $\epsilon_{\lambda_{max}}$ = 60 000 M^{-1} cm^{-1} in all cases, though the literature values for an assortment of simple dipyrrins vary widely. (a) A hexaalkyl meso-unsubstituted dipyrrin has ϵ_{490nm} = 63 100 M^{-1} cm^{-1} when protonated, ϵ_{450nm} = 20 000 M^{-1} cm^{-1} in the neutral form, and ϵ_{500nm} = 158 000 M^{-1} cm^{-1} in the zinc complex: Granick, S.; Gilder, H. In *Advances in Enzymology*; Nord, F. F., Ed.; Interscience Publishers: N. Y., 1947; Vol. 7, pp 305–368. (b) 2,2′,4,4′-Tetramethyl-3,3′-diethyldipyrrin perchlorate in dioxane: λ_{max} 485 nm; ϵ_{485} = 83 000 M^{-1} cm^{-1}. The free base: λ_{max} 442 nm; ϵ_{442} = 21 000 M^{-1} cm^{-1}. The zinc complex: λ_{max} 503 nm; ϵ_{503} = 150 000 M^{-1} cm^{-1}. Mauzerall, D.; Granick, S. *J. Biol. Chem.* **1958**, *232*, 1141–1162. (c) 5,5′-Dicarboxy-*meso*-[*p*-(dimethylamino)-phenyl]dipyrrin perchlorate in methanol: λ_{max} 540 nm; ϵ_{540} = 72 000 M^{-1} cm^{-1}. Morgan, L. R.; Schunior, R. *J. Org. Chem.* **1962**, *27*, 3696–3697. (d) *meso*-Phenyl-3,3′,4,4′,5,5′-hexamethyl-2,2′-dipyrrin in ethanolic hydrogen bromide: λ_{max} 516 nm; ϵ_{516} = 159 400 M^{-1} cm^{-1}. The bis(dipyrrin) zinc(II) complex: λ_{max} 507 nm; ϵ_{507} = 307 600 M^{-1} cm^{-1}. Dolphin, D. *J. Heterocycl. Chem.* **1970**, 275–283. (e) Bis[5-(*o*,*o*′-dichlorobenzyl)-*meso*-(2,6-dichlorophenyl)dipyrrin] zinc(II): λ_{max} 504 nm; ϵ_{504} = 180 000 M^{-1} cm^{-1}. Hill, C. L.; Williamson, M. M. *J. Chem. Soc., Chem. Commun.* **1985**, 1228–1229. (f) Copper(II) complexes of 3,3′,4,4′,5,5′-hexamethyldipyrrin, 3,3′,5,5′-tetramethyldipyrrin, and 3,4,5-trimethyldipyrrin in chloroform each gave λ_{max} 450–500 nm with $\epsilon \simeq$ 55 000 M^{-1} cm^{-1}: Murakami, Y.; Sakata, K. *Inorg. Chim. Acta* **1986**, *2*, 273–279.

(13) Cense, J.-M.; Le Quan, R.-M. *Tetrahedron Lett.* **1979**, 3725–3728.

(14) Suslick, K. S.; Fox, M. M. *J. Am. Chem. Soc.* **1983**, *105*, 3507–3510.

(15) The product distribution following a 1-h condensation (25 °C, 10^{-2} M 9-anthraldehyde and pyrrole in $CHCl_3$, 3.3×10^{-3} M BF_3) consisted of 10% 9-anthraldehyde, 8% dipyrrins, and a variety of additional unidentified components. After condensation for 1 h at 61 °C, only 5% 9-anthraldehyde remained unreacted but the yield of dipyrrins had increased to 13%. The yield of porphyrin was <1% after oxidation with DDQ or TCQ (as estimated by the presence of a small amount of characteristic porphyrin fluorescence), but no porphyrin product could be isolated. Further variation in reaction conditions (longer condensation times, use of TFA catalysis, oxidation in refluxing toluene) gave no improvements.

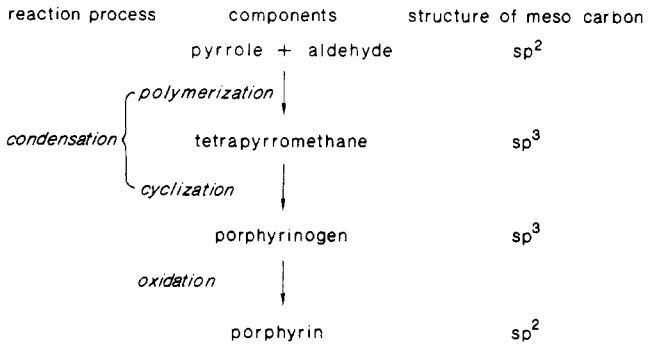
(16) Personal communication from Prof. T. G. Traylor.

Table V. Ortho-Substituted Tetraphenylporphyrins[a]

benzaldehyde	porphyrin[b]	reactn condtns: solvent, cond temp (°C), oxid temp (°C) CH_2Cl_2, 25, 25 (DDQ)	$CHCl_3$ 25, 25 (DDQ)	$CHCl_3$ 25, 61 (TCQ)[c]	$CHCl_3$ 61, 25 (DDQ)	$CHCl_3$ 61, 61 (TCQ)[c]	isolated yield,[d] %
2,4,6-$(CH_3)_3$	**6a**	0	31	32	17	21	29
2,4,6-$(CH_3O)_3$	**6b**	0	3.7	10	12	15	11
2,6-Cl_2	**6c**	50	14	16	29	30	24
2,3,4,5,6-F_5	**6d**	40	9.4	6.8	28	9.2	25
2,6-F_2	**6e**	52	35	39	53	55	46
2-EtO	**6f**	3.3	25	25	3.8	0	37
2-CH_3O	**6g**	3.7	38	37	3.7	4.3	20
2-CH_3	**6h**	26	50	50	17	10	45
2-CF_3	**6i**	43	1.4	0.3	33	34	35
2-F	**6j**	24	23	25	36	37	29
2-Cl	**6k**	27	19	21	37	39	28
2-Br	**6l**	30	21	23	36	38	24
2-O_2N	**6m**	27	6.4	10	7.2	19	10
1-naphthaldehyde	**6n**	22	52	30	0.9	1.1	41
2-methoxy-1-naphthaldehyde	**6o**	9	28	22	6.7	5.5	38

[a] The reactions were performed with 3.3 mM BF_3·OEt_2. The yield of dipyrrins after 1 h of condensation in $CHCl_3$ was 0.1–0.4% (25 °C) and ≤4% (61 °C), except for **1a** (5% at 25 °C and 20% at 61 °C (1 h)) and **1b** (30% at 25 °C and 18% at 61 °C (1 h)).[12] The porphyrin yields were determined spectroscopically (see Experimental Section for extinction coefficients) following removal of an aliquot and oxidation at 25 °C (DDQ) or after bulk oxidation for 1 h at 61 °C (TCQ). [b] See ref 27 for porphyrin literature references. [c] TCQ is 2,3,5,6-tetrachloro-1,4-benzoquinone (*p*-chloranil). [d] Preparative reactions were carried out (100-mL scale) by using the conditions found optimal in the survey reactions in $CHCl_3$.

Steric hindrance by substituents in the aldehyde moiety can subvert the reaction at the steps where structural changes occur:



Polymerization converts the configuration of the aldehyde carbon from sp^2 to sp^3 and juxtaposes two pyrrole units with the aldehyde nucleus. *Cyclization* of the tetrapyrromethane does not involve rehybridizations but is subject to conformational effects of aldehyde substituents. *Oxidation* converts the four meso carbons from sp^3 back to sp^2 configurations, requiring relaxation of the porphyrinogen into the planar porphyrin.

When an aldehyde fails (or reacts poorly) to give the porphyrin, it is difficult to ascertain whether this failure derives from maladjusted reaction parameters or from intrinsic structural limits imposed by the aldehyde substituents. We first discuss the reaction conditions found optimal for TMP and the reactivity patterns for various aldehydes and then attempt to isolate specific substituent structural effects.

I. Reaction Conditions. I.1. Catalysis. The mesitaldehyde–pyrrole condensation exhibits exacting catalytic requirements, but when these conditions are satisfied, steric hindrance in mesitaldehyde virtually disappears. Ethanol and BF_3 function as cocatalysts, as shown unequivocally by omission and reconstitution experiments. The reaction is dependent on the ratio of ethanol to BF_3, proceeding with as little as 0.1% ethanol (17 mM) and passing through a yield maximum at 0.75% ethanol (Table II). Cocatalysis with BF_3 and hydroxy compounds has been documented in the cationic polymerizations of cyclic ethers and acetals and in the isomerizations of alkenes. As in the mesitaldehyde–pyrrole case, these cocatalytic phenomena are highly dependent on the nature and concentrations of the Lewis acid and the hydroxy compound, the type of monomer and solvent, and other experimental variables.[17]

The major source of reactivity difference between benzaldehyde and mesitaldehyde is that the carbonyl in mesitaldehyde is over 100 times more basic (due to steric destabilization of the planar resonance form),[11] hence the stronger affinity of mesitaldehyde for BF_3. In the presence of ethanol, mesitaldehyde and benzaldehyde show similar apparent binding affinities and similar reactivities. Though the displacement of BF_3 from the complex is facilitated in the presence of ethanol (Table III), the addition of ethanol also inevitably results in BF_3 ethanolysis. One interpretation of the cocatalysis data is that the catalytic act does not result from polarization of the carbonyl through Lewis acid–base complexation,[18] but involves instead a Brønsted acid derived from BF_3 and ethanol.[19] An

(17) Cocatalysis effects are mechanistically rich. The polymerization of oxetanes in halomethane solvents does not occur under anhydrous conditions, but requires small amounts of water to proceed.[17a] The rate of polymerization can be quite sensitive to the concentration of cocatalysts. In the polymerization of oxacyclobutane (1.6 M) and BF_3 (0.1 M), for example, the rate passes through a maximum with an added H_2O concentration of 30 mM.[17b] Similarly, ethanol, acetic acid, or water function as effective cocatalysts with BF_3 in the polymerization of trioxane.[17c] The cocatalytic effect could be suppressed by addition of diethyl ether, presumably due to displacement of the BF_3·XH cocatalyst complex.[17c] Such exchange reactions of BF_3 with ethers are well-known.[17d] Cocatalysis was also observed in the cis–trans isomerization of 2-butene in ethylene chloride. For given concentrations of BF_3, the rate of isomerization was very sensitive to the added water concentration, with maximal rates observed at 2:1 BF_3:H_2O ratios and poisoning of the reaction at high H_2O concentrations.[17e] A fundamental understanding of the catalysis of cationic polymerization is not yet available, in spite of extensive studies.[17f] (a) Farthing, A. C.; Reynolds, R. J. W. *J. Polym. Sci.* **1954**, *12*, 503–507. (b) Rose, J. B. *J. Chem. Soc.* **1956**, 546–555. (c) Miki, T.; Higashimura, T.; Okamura, S. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 2480–2485. (d) Penczek, S.; Kubisa, P.; Matyjaszewski, K. *Adv. Polym. Sci.* **1980**, *37*, 28–32. (e) Eastham, A. M. *J. Am. Chem. Soc.* **1956**, *78*, 6040–6042. (f) Inoue, S.; Aida, T. In *Ring-Opening Polymerization*; Ivin, K. J., Saegusa, T., Eds.; Elsevier: 1984; Vol. 1, pp 185–298. Schulz, R. C.; Hellermann, W.; Nienburg, J. In *Cyclic Polymers*; Semlyen, J. A., Ed.; Elsevier: 1986; pp 369–460. Penczek, S.; Kubisa, P.; Matyjaszewski, K. *Adv. Polym. Sci.* **1985**, *68/69*.

(18) Reetz, M. T.; Hüllmann, M.; Massa, W.; Berger, S.; Rademacher, P.; Heymanns, P. *J. Am. Chem. Soc.* **1986**, *108*, 2405–2408.

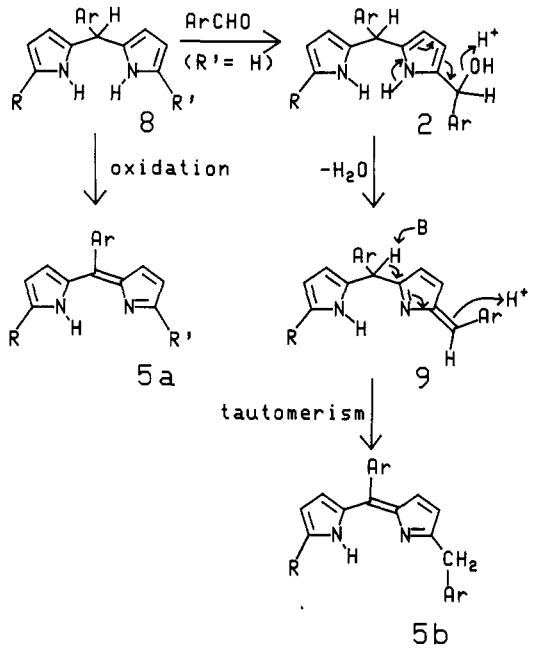


Figure 3. Proposed routes for dipyrrin formation.

alternative explanation is that acetals are involved. These data do not distinguish the detailed catalytic mechanism and the precise nature of the catalyst. However, the effect of proton donors is not specific to ethanol, as acetic acid and *tert*-butyl alcohol also resulted in reaction (Table II). Furthermore, TMP can be synthesized in the absence of alcohol at higher reactant concentrations (Table IV). These experiments rule out exclusive mechanisms proceeding with a BF_3–ethanol derived Brønsted acid or via acetals. Recent reports describe syntheses of TMP in 20% yield using BF_3–CH_3OH (1.8–3.6 mM)[20] and in 30% yield using 0.2 mM BF_3·OEt_2 in a 20-h reaction.[21] There undoubtedly exist a variety of reaction conditions that facilitate the formation of tetramesitylporphyrinogen from mesitaldehyde and pyrrole. Finally, it is noteworthy that other examples have been found of evanescent steric hindrance in the mesityl family in the face of improved catalysis.[22]

I.2. Dipyrrin Shunt. A truly benign catalyst in the porphyrin reaction would provide polypyrromethane and porphyrinogen formation while avoiding dipyrrin formation (Figure 1). In some cases dipyrrin formation can be the dominant side reaction, resulting in structures (**5b**) terminating chain growth. The decreased yield of TMP at higher acid concentration, for example, is accompanied by a dramatic increase in dipyrrin formation (Figure 2), presumably due to catalyst-induced tautomerism (**9** → **5b**) rather than from oxidation (**8** → **5a**) (Figure 3). The decrease in TMP yield with increasing temperature is also accompanied by increased dipyrrin formation (Table I). The Rothemund reaction of pyrrole, 2,6-dichlorobenzaldehyde, and zinc acetate in refluxing collidine (171 °C) afforded the zinc–porphyrin in 3.7% yield and a bis(dipyrrin)–zinc complex in 40% yield containing structures identical with **5b**.[12e] Similar dipyrrins were isolated from the reaction with mesitaldehyde.[23] The product distribution is reversed at room temperature, where reaction of 2,6-dichlorobenzaldehyde gives dipyrrins in 2% yield and the porphyrin in 50% yield (Table V).

Table VI. Substituent Size and Porphyrin Yield

ArCHO substituent	effective radius,[a] Å	porphyrin yield,[b] % 2	2,6
OCH_3	1.52	38	15
NO_2	1.61	27	0
phenyl	1.62	–	0
Cl	1.73	39	50
CH_3	1.80	50	32
Br	1.86	38	–
CF_3	2.2	43	0
1-naphthaldehyde		52	
2-methoxy-1-naphthaldehyde		28	
9-anthraldehyde		0	

[a] The effective radii are derived from experimental measures of the rotational barriers in ortho-substituted biphenyls.[24] [b] The yield values are the highest observed under any experimental conditions in Table V. See text for discussion.

I.3. Reactivity Patterns. Each aldehyde is expected to have an individualized reactivity pattern, especially since reactivity differences can be amplified in a multistep reaction. Indeed, slight variations in catalysis, temperature, and oxidant gave greater than 10-fold changes with aldehydes **1a,b,f,g,i,n**, 2–4-fold changes with aldehydes **1c,d,h,m,o**, but almost no change (<2-fold) with aldehydes **1e,j–l** (Table V). Synergistic effects of BF_3 and ethanol were observed for the ortho-substituted alkoxy- and alkylbenzaldehydes as well as the naphthaldehydes. 2,6-Dichlorobenzaldehyde and pentafluorobenzaldehyde gave slightly higher yields without added ethanol, and 2,6-difluorobenzaldehyde and the remaining monosubstituted aldehydes reacted indifferently to the presence of ethanol. Aldehydes substituted with electron-releasing groups (**1a,f–h**) generally gave higher yields with 25 °C condensation, with **1b** as the only exception. Aldehydes substituted with electron-withdrawing groups (**1c–e,i–m**) fared much better upon condensation at 61 °C. In general, little preference was observed for oxidant, except that pentafluorobenzaldehyde proceeded better with DDQ and 2,4,6-trimethoxybenzaldehyde gave better results with TCQ.

II. Structural Factors. We focus on structural models of porphyrinogens to gain insight into substituent effects on porphyrin yields, with the caveat that this ignores preceding and subsequent intermediates and reaction steps. Substituents can impose both kinetic barriers and thermodynamic limits to the conversion of aldehyde to porphyrinogen. If the porphyrinogen is not strained and is more stable than the reactants, the reaction occurs spontaneously when catalytic conditions are found that permit kinetic barriers to be surmounted. Improved catalytic conditions are not alone sufficient for the reaction to proceed, however, if the aldehyde substituents cause a porphyrinogen to be so strained that it lies at higher energy than the reactants. The formation of tetramesitylporphyrinogen illustrates the former case, where minimal intrinsic structural limitations are present but exacting catalysis is essential to overcome kinetic barriers.

(19) A simple example of a Brønsted acid formed by dissociation of the BF_3·XH complex is shown in eq 2, where XH is the cocatalyst.

$$BF_3{\cdot}OR_2 + XH \rightleftharpoons BF_3{\cdot}XH + OR_2 \quad (1)$$

$$BF_3{\cdot}XH \rightleftharpoons BF_3X^- + H^+ \quad (2)$$

See: Collins, G. L.; Greene, R. K.; Berardinelli, F. M.; Ray, W. H. *J. Polym. Sci.: Polym. Chem. Ed.* **1981**, *19*, 1597–1607. Wamser, C. A. *J. Am. Chem. Soc.* **1951**, *73*, 409–416.

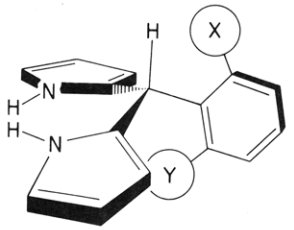
(20) Kihn-Botulinski, M.; Meunier, B. *Inorg. Chem.* **1988**, *27*, 209–210.

(21) van der Made, A. W.; Hoppenbrouwer, E. J. H.; Nolte, R. J. M.; Drenth, W. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 15–16.

(22) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017–7036.

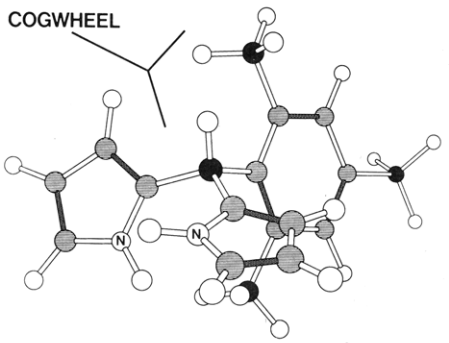
(23) Marchon, J.-C.; Ramasseul, R.; Ulrich, J. *J. Heterocycl. Chem.* **1987**, *24*, 1037–1039.

Scheme I. 5-Aryldipyrromethane[a]



[a] A $^3/_8$ segment of the tetraarylporphyrinogen.

Scheme II



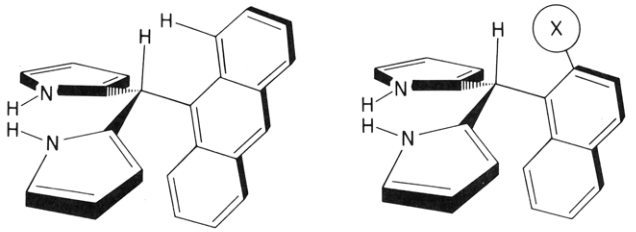
The comparison of porphyrin yield data and substituent size can be used to draw distinctions between inappropriate experimental conditions and intrinsic structural limitations. Table VI contains a compilation of the best porphyrin yields observed under any conditions examined in Table V. One measure of substituent size is the effective radius obtained from experimentally measured rotational barriers in ortho-substituted biphenyls.[24] These values must be used with care, as steric effects are dependent on the size and shape of a substituent as well as the environment with which it interacts. In the porphyrinogen, one ortho substituent (X) faces the meso hydrogen, and the second substituent (Y) juts into the groove below the tetrahedral meso carbon (Scheme I). These two interactions are also seen in the minimal energy conformation of 5-mesityldipyrromethane, the structural motif of tetramesitylporphyrinogen.[25] One methyl group is packed snugly into the lower groove, and the second methyl group docks in a cogwheel fashion with the meso hydrogen (Scheme II). The effective radii (Table VI) should roughly estimate the interaction of the ortho group at the meso hydrogen, because the geometry of an *o*-biphenyl interaction is similar to that of the ortho substituent with the meso hydrogen in the porphyrinogen. But the placement of a substituent into the groove below the tetrahedral meso carbon depends on the shape of a substituent and has a different trajectory than a biphenyl eclipsing motion, and this interaction is not expected to be measured by the effective radii in Table VI.

Aldehydes bearing ortho substituents "smaller" than the methyl group should react with equal or greater yield, and those that react poorly indicate inappropriate experimental conditions rather than intrinsic steric constraints. The nitro group is smaller than the methyl group; thus the failure of 2,6-dinitrobenzaldehyde reflects factors other than steric effects. The methoxy group also is small, and the low yield obtained with 2,4,6-trimethoxybenzaldehyde is attributed to its propensity to form dipyrrins (Table V).

(24) Bott, G.; Field, L. D.; Sternhell, S. *J. Am. Chem. Soc.* **1980**, *102*, 5618–5626.

(25) Energy-minimized by using the program Alchemy (Tripos Associates) and plotted by using Chem 3D (Cambridge Scientific Computing).

Scheme III



This analysis suggests that experimental conditions should exist that support the reaction of 2,6-dinitrobenzaldehyde and afford improved yields with 2,6-dialkoxybenzaldehydes.

A distinction between limiting reaction conditions and limiting structural features cannot be made for 2,6-disubstituted aldehydes bearing substituents larger than the methyl group, the largest group for which the reaction succeeded. Nonetheless, we proceed with structural models to try to identify possible steric congestion in the porphyrinogen. Molecular models show that the meso hydrogen can accommodate all of the substituents in Table VI (OCH_3, NO_2, Ph, Cl, Br, CH_3, CF_3), and only the phenyl and trifluoromethyl groups do not fit well into the groove below the tetrahedral meso carbon. The phenyl group is larger than the methyl group, though the effective radius as measured in biphenyl rotations is smaller than that of the methyl group. The phenyl group does protrude tightly into the space below the tetrahedral meso carbon, but it is not clear whether the failure of 2,4,6-triphenylbenzaldehyde results from intrinsic steric limitations or inappropriate reaction conditions. Fluorine is larger than hydrogen, and though CF_3 forms a cogwheel about the meso hydrogen as does CH_3, the CF_3 group cannot be accommodated readily in the groove below the tetrahedral meso carbon. The reaction of 2-(trifluoromethyl)benzaldehyde succeeds (43%), but that of 2,6-bis(trifluoromethyl)benzaldehyde fails (0%); one CF_3 group can avoid steric interactions in the groove by cogwheeling with the meso hydrogen, but with two CF_3 groups, the steric interaction in the groove cannot be avoided.

9-Anthraldehyde and 1-naphthaldehyde have similar structures, but the former fails (0%) and the latter succeeds (52%). Molecular models of tetraanthrylporphyrinogen show that the 1-H is thrust into a severe eclipsing interaction with the meso hydrogen but the 8-H is unobstructed in the lower groove (Scheme III). Naphthaldehyde can avoid the meso hydrogen eclipsing interaction by rotation of the 8-H into the lower groove (Scheme III, X = H). The success of 2,4,6-trimethoxybenzaldehyde (albeit in moderate yield) shows that the methoxy group does not unduly eclipse the meso hydrogen (Scheme III, X = OCH_3), and therefore it is consistent that 2-methoxy-1-naphthaldehyde also reacts to give the porphyrin.

A comparison of yield data and substituent size is useful for reactions with substituents smaller than the largest one that has succeeded. This approach does not relate substituent size to porphyrinogen strain energy, and therefore an upper limit cannot be placed on intrinsic steric tolerances. Though models indicate that the porphyrinogens from 9-anthraldehyde, 2,6-bis(trifluoromethyl)benzaldehyde, and 2,4,6-triphenylbenzaldehyde appear sterically hindered, the structural limits to porphyrinogen formation are not yet known and these aldehydes may submit in good yield in the presence of improved reaction conditions, just as mesitaldehyde did. Molecular mechanics calculations ultimately should provide a more

quantitative treatment of substituent effects on porphyrinogen stability, thereby identifying the limits to which aldehydes can be ortho-functionalized for conversion via the porphyrinogen to the porphyrin.

Experimental Section

General. ^1H NMR spectra (300 MHz, General Electric GN 300NB), IR spectra (Nicolet 5DXB), absorption spectra (HP 8451A), and fluorescence spectra (Gilford Fluoro IV) were collected routinely. Extinction coefficients were obtained with an IBM 9430 spectrometer. Absorption and emission spectra were collected in CH_2Cl_2/ethanol (3:1). HPLC analyses were performed on a HP-1090 liquid chromatograph. Column chromatography was performed on neutral alumina and Florisil (Fisher, 60–100 mesh). Pyrrole was distilled at atmospheric pressure. Aldehydes were used as received from commercial sources (Aldrich, Fluka).

Solvents. CH_2Cl_2 (Fisher, reagent grade), $CHCl_3$ (Fisher certified A.C.S.), and CCl_4 (Baker) were distilled from K_2CO_3 and were stored over 4-Å molecular sieves. The commercially available $CHCl_3$ contained ethanol (0.75%) as a stabilizer. Ethanol was not removed by distillation from K_2CO_3. $CHCl_3$ was depleted of ethanol by first washing with an equal volume of water and drying over $CaCl_2$, followed by simple distillation from P_2O_5. The initial and final fractions were discarded, giving a 50% yield of purified $CHCl_3$.[26] All references to $CHCl_3$ in this paper pertain to $CHCl_3$ containing 0.75% ethanol (distilled from K_2CO_3), unless it is noted that ethanol-free $CHCl_3$ was used.

Acid Catalysts. Stock solutions of $BF_3{\cdot}OEt_2$ were prepared by diluting the commercially available $BF_3{\cdot}OEt_2$ from Aldrich (8.1 M) to 2.5 M in $CHCl_3$ or CH_2Cl_2, depending on the solvent used in the reaction. The 2.5 M stock solution of $BF_3{\cdot}OEt_2$ was then used in the synthetic procedures described here as well as in our previous communication.[9] Stock solutions remained viable for at least 2 weeks. BCl_3 (1 M in CH_2Cl_2) and trifluoroacetic acid were used as obtained from Aldrich.

Reaction Survey. For survey reactions, a 50-mL three-neck round-bottomed flask was charged with 25 mL of $CHCl_3$ (distilled from K_2CO_3) and equimolar quantities of aldehyde and pyrrole. No significant improvements were observed upon deaeration with N_2. The reaction vessel was shielded from ambient light.

Porphyrin yields were determined by removing aliquots from the reaction mixture and oxidizing with excess DDQ at room temperature, followed by absorption spectroscopy. Typical procedure: A 50-μL reaction aliquot was injected into 300 μL of 10^{-2} M DDQ in toluene, and then 50 μL of this oxidized solution was placed in 3 mL of CH_2Cl_2/ethanol (3:1) for absorption spectroscopy. The yield of porphyrin was determined by the intensity of the Soret band measured from the apex to the base of the red edge of the band. This eliminated the contribution of the polypyrromethene and quinone components, which exhibit a broad band in the 400–450-nm region. The ratio of DDQ quenching solution to the reaction aliquot was adjusted upward for condensations performed at 10^{-1} M, in order to keep the DDQ quantity in excess. Also, the reactions performed with high BF_3 concentrations often resulted in the porphyrin diacid. In these cases, triethylamine was added via syringe (~10 μL) to the cuvette solution in order to liberate the free-base porphyrin prior to quantitation. The Soret-band extinction coefficients used in yield determinations were 500 000 M^{-1} cm^{-1} (2-substituted benzaldehydes), 300 000 M^{-1} cm^{-1} (2,6-disubstituted benzaldehydes), and 427 000 M^{-1} cm^{-1} (mesitaldehyde).

In some instances, black precipitates formed upon DDQ oxidation, and in these cases the oxidation was better performed in the mixed solvent toluene/ethanol (3:1). This solvent affords improved solubility, but the addition of ethanol to give a 10^{-2} M solution of DDQ in toluene/ethanol (3:1) must be performed immediately prior to use, because high potential quinones such as DDQ react with alcohols. Both solvent systems gave identical yields.

The yield of dipyrrins during the condensation was determined by absorption spectroscopy of aliquots removed directly from the reaction vessel. An extinction coefficient of 60 000 M^{-1} cm^{-1} was used for the broad peak which occurs in the 450–520-nm region.[12]

Bulk oxidation of reaction mixtures was performed by adding a stoichiometric amount (3 equiv per porphyrinogen) of *p*-chloranil (TCQ) in powder form to the reaction vessel. The reaction mixture was then gently refluxed for 1 h. The survey reactions can be scaled up from 25 mL to 1 L without a decrease in yield.

Purification. Porphyrin purification could be accomplished in many cases by simply washing the crude dried reaction mixture with methanol. The crude reaction mixture was first neutralized with triethylamine (1 equiv) and then rotary evaporated to dryness. The dry powder was then placed on a filter (Whatman No. 1 qualitative, 5.5 cm) secured in a fritted-glass filter holder (Schleicher and Schuell GV 050/0 glass filter holder). The dry powder was washed with a series of small aliquots of absolute methanol under aspirator vacuum until the eluant was clear. Addition of large volumes of methanol usually caused loss of the finely powdered porphyrin. Porphyrins **6b,f,g,m–o** were not readily freed from non-porphyrin components by washing with methanol, but were purified by column chromatography on alumina with CH_2Cl_2 containing 1–2% ethyl acetate as the eluant.

Aldehyde–BF_3 Binding Experiments. Binding studies were performed of BF_3 with benzaldehyde and mesitaldehyde in three solvents, CH_2Cl_2, CH_2Cl_2 + 0.75% ethanol, and $CHCl_3$. Stock solutions of $BF_3{\cdot}OEt_2$ were prepared in CH_2Cl_2 or $CHCl_3$. Benzaldehyde was vacuum distilled, and mesitaldehyde was used as received (Aldrich). No precipitation was observed in these titrations. A representative procedure is given for mesitaldehyde in CH_2Cl_2. In a 1-cm quartz cell was placed 2.0 mL of a 3.5×10^{-5} M solution of mesitaldehyde (λ_{max} 266 nm; ϵ_{266} = 12 000 M^{-1} cm^{-1}, ϵ_{304} = 1500 M^{-1} cm^{-1}) in CH_2Cl_2. The addition of a large excess of $BF_3{\cdot}OEt_2$ (5 μL of an 8.1 M stock solution) gave saturation conversion to the BF_3–aldehyde complex (λ_{max} 304 nm; ϵ_{304} = 18 500 M^{-1} cm^{-1}, ϵ_{266} = 4000 M^{-1} cm^{-1}). A new solution of mesitaldehyde (3.5×10^{-5} M) was then titrated with 10-μL aliquots of $BF_3{\cdot}OEt_2$ (110 μL total, stock solutions 5×10^{-4} M and 5×10^{-3} M in CH_2Cl_2). The red-shifted absorption band of the complex was clearly distinguished from the major absorption peak of mesitaldehyde, permitting determination of the binding by straightforward two-component analysis using the four extinction coefficients for the bound and free aldehyde at 266 and 304 nm. An isosbestic point occurred at 281 nm.

Analogous experiments were performed with mesitaldehyde in $CHCl_3$ and CH_2Cl_2 + 0.75% ethanol. The extinction coefficients varied little from those observed in CH_2Cl_2. The titrations of benzaldehyde also were performed similarly. The extinction coefficients for benzaldehyde (λ_{max} 248 nm; ϵ_{248} = 12 000 M^{-1} cm^{-1}, ϵ_{282} = 1500 M^{-1} cm^{-1}) and the benzaldehyde–BF_3 complex (λ_{max} 282 nm; ϵ_{282} = 19 000 M^{-1} cm^{-1}, ϵ_{248} = 5900 M^{-1} cm^{-1}; lit. $\epsilon_{281.6}$ = 18 800 M^{-1} cm^{-1} (ref 10)) determined in CH_2Cl_2 were comparable to those of mesitaldehyde and its complex, respectively. The titrations of benzaldehyde (3.5×10^{-5} M) were slightly altered by two factors, however. First the absorption band of benzaldehyde at 248 nm was slightly clipped on the short wavelength edge by the absorptions of both CH_2Cl_2 and $CHCl_3$. Second, the titration of benzaldehyde in $CHCl_3$ and CH_2Cl_2 + 0.75% ethanol required the addition of large excesses of BF_3. The point of saturation conversion was difficult to determine clearly, because at high BF_3 concentrations (~0.1–1 M) the weak background absorption contributed by the BF_3 solution at 240 and 266 nm began to intrude on the absorption of the aldehyde and its com-

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plex. Therefore the extinction coefficient of the benzaldehyde–BF_3 complex (λ_{max} 282 nm) was assumed to be 19 000 M^{-1} cm^{-1}, in analogy with that determined for the benzaldehyde–BF_3 complex in CH_2Cl_2, and in accord with the relative invariance of the extinction coefficient of the mesitaldehyde–BF_3 complex in the three solvents.

***meso*-Tetramesitylporphyrin (6a).** A 2-L three-neck round-bottomed flask fitted with a septum, reflux condenser, and nitrogen inlet port was charged with 1 L of $CHCl_3$ (distilled from K_2CO_3), mesitaldehyde (1.475 mL, 10 mmol, 10^{-2} M), and pyrrole (694 μL, 10 mmol, 10^{-2} M). After the solution was purged with N_2 for 5 min, 1.32 mL of 2.5 M BF_3·OEt_2 (3.3 mmol, 3.3×10^{-3} M) was added via syringe. The room temperature reaction was monitored by removing 50-μL aliquots and oxidizing with excess DDQ, followed by absorption spectrophotometry. At the end of 1 h, *p*-chloranil (1.844 g, 7.5 mmol) was added in powder form and the reaction mixture was gently refluxed (61 °C) for 1 h. The reaction mixture then was cooled to room temperature, 1 equiv of triethylamine (3.3 mmol, 460 μL) was added, and the solution was rotary evaporated to dryness. The crude dry product was scraped from the flask, placed on a filter, and washed with methanol (~75 mL) until the filtrate was clear. The polypyrromethenes and quinone components are highly soluble in methanol and are removed with ease. The final product (576 mg, 29%) was greater than 95% pure as evidenced by TLC, HPLC, and absorption and fluorescence (excitation and emission) spectroscopy. λ_{abs} (log ε): 403 (sh), 418 (5.63, fwhm 10 nm), 480 (2.95), 514 (4.20), 547 (3.57), 590 (3.70), 647 nm (3.48). λ_{em}: 650, 714 nm. The extinction coefficients are the average of three determinations (compare with lit. log ϵ_{Soret} = 5.57,[2] 5.72[3]). ^1H NMR ($CDCl_3$, 300 MHz): δ −2.51 (br s, 2 H, NH), 1.85 (s, 24 H, *o*-CH_3), 2.62 (s, 12 H, *p*-CH_3), 7.27 (s, 8 H, *m*-ArH), 8.61 (s, 8 H, β-pyrrole).

***meso*-Tetrakis(2-ethoxyphenyl)porphyrin (6f).** A 250-mL, three-neck round-bottomed flask fitted with a condenser and nitrogen inlet port was charged with 100 mL of $CHCl_3$ (distilled from K_2CO_3). Samples of 2-ethoxybenzaldehyde (140 μL, 1 mmol, 10^{-2} M) and pyrrole (69 μL, 1 mmol, 10^{-2} M) were added, and the solution was stirred magnetically under a slow steady stream of nitrogen. After 5 min, BF_3·OEt_2 from a 2.5 M stock solution in $CHCl_3$ (132 μL, 3.3 mM) was added and the reaction mixture was allowed to proceed at room temperature. After 1 h, the yield was found to be 25% (assuming $\epsilon_{418} = 5 \times 10^5$ M^{-1} cm^{-1}) upon aliquot removal and oxidation with excess DDQ. At this point, oxidation was initiated by the addition of *p*-chloranil (184 mg, 0.75 mmol, 3 equiv per porphyrinogen), and the reaction vessel was immersed in an oil bath preheated to 65 °C. After a 1-h oxidation period, the reaction mixture was cooled to room temperature and 1 equiv of triethylamine (46 μL, 3.3 mM) was added. The crude reaction mixture was transferred to a 200-mL round-bottomed flask, 750 mg of Florisil was added, and the solvent was removed via rotary evaporation. The resulting dry powder was placed on top of a dry alumina column (1 × 15 cm). The porphyrin eluted quickly with CH_2Cl_2 containing 1–2% ethyl acetate, affording 73 mg (37% yield) of the title compound in greater than 95% purity, as evidenced by TLC (silica, CH_2Cl_2 or CH_2Cl_2/petroleum ether), NMR, absorption and fluorescence (excitation and emission) spectroscopy. ^1H NMR ($CDCl_3$): δ −2.65 (br s, 2 H, NH), 0.61, 0.7 (m, 12 H, CH_3), 3.90, 3.97 (m, 8 H, OCH_2), 7.30, 7.34 (m, 8 H, ArH), 7.69, 7.75 (m, 4 H, ArH), 7.97, 8.03 (m, 4 H, ArH), 8.74 (s, 8 H, β-pyrrole). λ_{abs}: 418, 514, 548, 590, 644 nm. λ_{em}: 650, 712 nm.

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Supplementary Material Available: ^1H NMR spectral data and absorption spectral data (λ_{max} values only) of compounds **6b–e** and **6g–o** (3 pages). Ordering information is given on any current masthead page.

Rearrangement of 1-Methyl-2-(substituted-phenyl)piperidinium 1-Methylides in a Neutral Medium

Naohiro Shirai, Fumihiko Sumiya, Yoshiro Sato,* and Mikiko Hori

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467, Japan

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Reaction of 1-methyl-1-[(trimethylsilyl)methyl]-2-(substituted-phenyl)piperidinium iodides (**3**) with cesium fluoride in DMF gave good yields of 2-methyl-1,3,4,5,6,11a-hexahydro-2*H*-2-benzazonine derivatives (**5**), which are regarded as unstable intermediates in the Sommelet–Hauser rearrangement of ammonium ylides (**4**) to 2-methyl-2,3,4,5,6,7-hexahydro-1*H*-2-benzazonine derivatives (**6**). Compound **5** was converted on heating to two isomers, (*E*)-*N*,*N*-dimethyl-5-(substituted-phenyl)-4-pentenylamines (**8**) and 1-methyl-3-(substituted-phenyl)-perhydroazepines (**9**), and it was aromatized to **6** in the presence of potassium hydroxide. Related reactions are also described.

Introduction

The Sommelet–Hauser rearrangement is well known as a regioselective rearrangement of benzyldialkylammonium *N*-methylides to give ortho-substituted benzylamine derivatives.[1] Hauser et al.[2] reported that this rearrangement is also applicable to a ring expansion reaction giving cyclic amines. For example, 2-methyl-2,3,4,5,6,7-hexahydro-1*H*-2-benzazonine (**6a**) and its analogues (**6b** and **6c**) were prepared in high yields by the ylide reaction of 1,1-dimethyl-2-phenylpiperidinium iodides with sodium amide in liquid ammonia.[2,3]

We previously reported that the fluoride ion assisted desilylation of (substituted-benzyl)dialkyl[(trimethylsilyl)methyl]ammonium halides gave high yields of the Sommelet–Hauser rearrangement products in a nonbasic medium at room temperature.[4] Application of this ylide

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