SYNTHESIS AND CHARACTERIZATION OF A "BIS-POCKET" PORPHYRIN

BY

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THIS IS TO CERTIFY THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

JOANN L. STEINHARDT

ENTITLED

SYNTHESIS AND CHARACTERIZATION

OF A "BIG-FOOTED" PHILLYMIN

IS APPROVED BY ME AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE

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HEAD OF DEPARTMENT OF CHEMISTRY
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# TABLE OF CONTENTS

I. INTRODUCTION ................................................. 1
   1) O₂ Binding .................................................. 1
   2) O₂ Activation and Hydrocarbon Hydroxylation ....... 1
   3) Interaction of Oxidants and Fe(III) Porphyrin Complexes .................................................. 5
II. RESULTS AND DISCUSSION ...................................... 7
III. EXPERIMENTAL .................................................. 15
   General ................................................................... 15
   2,4,6-triphenylbromobenzene ................................ 15
   2,4,6-triphenylbenzaldehyde .................................. 16
   meso-tetrakis(2,4,6-triphenylphenyl)porphyrin ........ 18
   Dimethylsiloxane .................................................. 20
   Iodo-tetrakis(2,4,6-triphenylphenyl)porphyrinato-
   iron(III) .............................................................. 21
IV. REFERENCES ....................................................... 22
LIST OF FIGURES:

Figure 1 ----- Hydroxylation mechanism ----------------- 3
Figure 2 ----- NIH shift ------------------------------- 4
Figure 3 ----- Hydroperoxidase Catalytic Cycle ------ 6
Figure 4 ----- Spectra of H$_2$TTPPP and (H$_4$(TTPPP))$^{2+}$ --- 13
Figure 5 ----- Spectrum of FeT TPPPI ------------------- 14

LIST OF TABLES:

Table 1 ----- Conditions for synthesis of $\eta_3$CCHO ----- 9
Table 2 ----- Conditions for synthesis of H$_2$TTPPP ---- 10
Table 3 ----- Yields from $\eta_3$CCHC reaction ------------- 17
SYNTHESIS AND CHARACTERIZATION
OF A "BIS-POCKET" Porphyrin

I. INTRODUCTION

1. O2 Binding

The synthesis and characterization of various iron dioxygen complexes has recently been accomplished. A good review of such complexes can be found in reference 1 and references cited therein. The formation of a μ-oxo Fe(III) dimer is a major obstacle to reversible oxygen binding in many reported systems. With respect to porphyrinatoiron complexes, one method for the prevention of irreversible oxidation has been the design of sterically protected porphyrins. Two notable examples of this type of porphyrin are the "picket fence" and capped complexes of Collman2 and Baldwin3, respectively. This paper introduces the synthesis of a "bis-pocket" porphyrin, meso-tetrakis(2,4,6-triphenylphenyl)porphyrin, or \( \text{H}_2\text{TrP} \), a complex with a protective "pocket" on both faces of the porphyrin plane. This steric protection should facilitate reversible oxygen binding by preventing two metalloporphyrins from approaching near enough to form the μ-oxo dimer.

2. O2 Activation and Hydrocarbon Hydroxylation

Another area of particular interest is the study of O2 activation and hydrocarbon hydroxylation via models of cytochrome P-450. (The monooxygenase cytochrome P-450 is associated with a diverse assortment of biological functions as well as the hydroxylation of a wide variety of substrates.) Investi-
ations with analogs of various intermediates of the enzymatic cycle indicate the presence of a thiol or thiolate axial ligand\textsuperscript{4a,5}. Much related work has also been devoted to model studies of analogs of the cytochrome P-450 hydroxylation cycle. Sakurai recently proposed that the thiolate-heme iron linkage is retained during aniline hydroxylation and he subsequently introduced a possible hydroxylation mechanism\textsuperscript{6}. Groves presents a thorough review of the current understanding in this area\textsuperscript{5} and suggests an intermediate iron bound oxidant in model system aliphatic hydroxylations. His hydroxylation mechanism is shown in figure 1.\textsuperscript{7} More recently he has reported oxo-Cr(V) and oxo-Mn(V) porphyrin complexes that resemble the proposed oxo-Fe(V) species\textsuperscript{9,9}. Other investigators have recently carried out related hydroxylation studies with various systems\textsuperscript{10}. No known model transition metal system shows the NIH shift (i.e. shift of D, T or an alkyl group from a \textit{para} to a \textit{meta} position during ring hydroxylation of a substituted benzene. See figure 2.)\textsuperscript{11} which is characteristic of cytochrome P-450 hydroxylation. Recently, however, Castle et al\textsuperscript{12} have demonstrated the NIH shift during the non-enzymatic hydroxylation of aromatic compounds by oxy-radicals.

Synthetic analogs of peroxidase and cytochrome P-450 intermediates are still lacking. The isolation and studies of FeTFPP-I should help clarify some of these issues. In particular, the demonstration of the NIH shift during aromatic hydroxylation by an iron based oxidant is desirable for a comparison to the cytochrome P-450 shift. Also, the reactions of various reductants with the C2-Fe complex and the effect of
FIGURE 1

Hydroxylation mechanism?
FIGURE 2

NIM SHIFT

$R = ^2H, ^3H, $alkyl
axial ligation (in particular thiol and thiolate ligation due to their precedent in the cytochrome P-450 system) will add to the understanding in this area. Finally, because the FeIITrpIII molecule has well protected, symmetrical pockets, an attempt at isolating and characterizing an iron-oxo complex or its precursor, an C2-Fe-thiol(ate) complex would be instructive.

3. Interaction of Oxidants and Fe(III) Porphyrin Complexes

The importance of the hydroperoxidases (catalase, peroxidase, and haloperoxidase) as detoxifying agents and regulators of biological processes is well documented in reference 13 and references cited therein. The catalytic cycle of these enzymes is shown in figure 3. Of particular interest are the two metastable intermediates, compound I and compound II. Compound I is formed from the resting Fe(III) state by reaction with oxidants and is two oxidizing equivalents above Fe (III). It is generally accepted as an oxyferryl (C=Fe(IV)) with the other oxidizing equivalent located as a Φ-radical cation on the porphyrin in most cases13. (Cytochrome c peroxidase is an exception14.) Compound II is produced by a peroxidase assisted one electron reduction of compound I. It is presumably an oxyferryl, or a ferryl hydroxide (OC-Fe(IV)).13

Model systems have been used to study these compounds15. For iron, the porphyrin radical cation has not been produced by electrochemical oxidation of ferric hemes15b. Instead, the porphyrinateiron(IV)X2 species (where X = Cl-, Br-) is produced. The isolation of a Φ-radical cation during the
Hydroperoxidase Catalytic Cycle

\[ \text{Compound I} \rightarrow \text{Compound II} \rightarrow \text{Compound III} \]

\[ \text{P}_{450} \text{ Chem.} \]

\[ \text{A}^- + \text{H}_2\text{O} \]

\[ \text{Fe}^{III} \]

\[ \text{O}_2 + \text{H}_2\text{O} \rightarrow \text{H}_2\text{O}_2 \]

\[ \text{Compound X} \]

\[ X^- = \text{I}^-, \text{Br}^-, \text{Cl}^-, \text{SCN}^- \]

\[ \text{AH} = \text{phenols, NO}_2^-, \text{ascorbate, N}_3^- \]

\[ \text{Fe(CN)}_6^{3-}, \text{cyt c(red)}, \ldots \]

\[ [0] = \text{H}_2\text{O}_2, \text{ROOH, RCOOH} \]
oxidation of the proposed iron porphyrinate complex is possible. Also, kinetic studies of oxidant reactions with the FeTTPPP complex should not be thwarted by the formation of a μ-oxo dimer as in previous ferric porphyrins. The steric bulk on both sides of the porphyrin plane should prevent two iron atoms from approaching near enough to form the dimer. Finally, the steric encumbrance of the meso-methylene positions should slow the oxidative degradation of this porphyrin. This should further ease the complications of previous kinetic studies. The isolation of crystalline analogs of compound I and compound II is a further goal in the studies of H₂TTPPP.

**II. RESULTS AND DISCUSSION**

The preparation of H₂TTPPP was accomplished with the following reaction sequence:

\[
\begin{align*}
\text{Br}_2 & \xrightarrow{\text{CS}_2} \quad \text{1-n-BuLi} & \quad \text{pyrrole} & \quad \text{H}_2\text{TTPPP} \\
\text{CH}_3\text{CO}_2\text{H} & \quad \text{2-Diep} & \\
\end{align*}
\]

meso-tetrakis(2,4,6-triphenylphenyl)porphyrin (H₂TTPPP)

The first step in the synthesis, the bromination of triphenylbenzene (C₆H₃Br) occurs in near quantitative yields (i.e., >95%).
In the next step, the formulation of $\mathcal{C}_3\mathcal{Br}$, various reaction conditions were tried in order to optimize conditions. Initially toluene was chosen as the solvent (reaction #1, table #1). After addition of the n-BuLi, the solution was cloudy and remained cloudy until the DHP quenching. Upon cooling to room temperature, a small amount of white precipitate formed. Presumably a side reaction with the solvent was occurring. G.C. analysis of the product showed 35.6% $\mathcal{C}_3\mathcal{Br}$ and 6.3% of the desired product, triphenylbenzaldehyde ($\mathcal{C}_3\mathcal{C}_6$). The remainder of the peaks observed on the gas chromatograph were not identified but presumably correspond to side reactions. One side reaction could be the competing lithiation of toluene. Thus the small yield of $\mathcal{C}_3\mathcal{C}_6$ is not surprising.

The next solvent used was diethylether (reactions 2 & 3, table 1). This system was run both at room temperature (25°C) and refluxing temperature (35°C). Both reactions turned cloudy after addition of the n-BuLi and remained cloudy after the quenching with DHP. This presumably was due to the poor solubility of triphenylbromobenzene in the ether since no competing reactions could occur with diethylether. The room temperature reaction resulted in 40.5% $\mathcal{C}_3\mathcal{Br}$ and 28.6% $\mathcal{C}_3\mathcal{C}_6$. The refluxing solution yielded 33.0% $\mathcal{C}_3\mathcal{Br}$ and 27.3% $\mathcal{C}_3\mathcal{C}_6$ upon GC analysis.

The final solvent chosen was benzene (reactions 4-7, table 1). Benzene was chosen because of the high solubility of $\mathcal{C}_3\mathcal{Br}$ in it and because of the apparent lack of solvent side reactions. The concentration of the solution was varied over a large range to optimize the conditions. All reactions were carried out at
<table>
<thead>
<tr>
<th>REACTION</th>
<th>SOLVENT</th>
<th>CONCENTRATION (g per 100g)</th>
<th>TEMPERATURE</th>
<th>$\Phi_3\mathcal{C}_1$*</th>
<th>$\Phi_3\mathcal{C}_3\mathcal{C}_6$*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>toluene</td>
<td>0.173</td>
<td>111°C</td>
<td>35</td>
<td>6.3%</td>
</tr>
<tr>
<td>2</td>
<td>diethyl ether</td>
<td>0.104</td>
<td>25°C</td>
<td>40.6%</td>
<td>28.6%</td>
</tr>
<tr>
<td>3</td>
<td>diethyl ether</td>
<td>0.130</td>
<td>35°C</td>
<td>33.0%</td>
<td>27.3%</td>
</tr>
<tr>
<td>4</td>
<td>benzene</td>
<td>0.173</td>
<td>80°C</td>
<td>37.9%</td>
<td>50.5%</td>
</tr>
<tr>
<td>5</td>
<td>benzene</td>
<td>0.130</td>
<td>80°C</td>
<td>37.0%</td>
<td>46.9%</td>
</tr>
<tr>
<td>6</td>
<td>benzene</td>
<td>0.519</td>
<td>80°C</td>
<td>32.0%</td>
<td>48.9%</td>
</tr>
<tr>
<td>7</td>
<td>benzene</td>
<td>0.346</td>
<td>80°C</td>
<td>39.3%</td>
<td>50.5%</td>
</tr>
</tbody>
</table>

*G.C. yields

### TABLE 1

Conditions for synthesis of $\Phi_3\mathcal{C}_3\mathcal{C}_6$

reflux (80°C). The observed yields are shown in table 1 for the various concentrations. The highest yield occurs for a concentration of 0.346 g. This produced 39.3% $\Phi_3\mathcal{C}_3\mathcal{C}_6$ (which can be rebranched and, hence, reused for this reaction) and 50.5% yield of the desired $\Phi_3\mathcal{C}_3\mathcal{C}_6$. These conditions were, consequently, used in all subsequent reactions.

Isolation of the product was initially accomplished via gravity column chromatography but due to the efficiency of the flash chromatography technique¹, it became the preferred technique. The first band collected is the initial starting material of the reaction sequence, triphenylbenzene, and was recovered for rebranched. The second band is the product ($\Phi_3\mathcal{C}_3\mathcal{C}_6$). The baseline bands were separated by increasing the polarity of the solvent system (from 20% CH$_2$Cl$_2$ in hexanes to straight CH$_2$Cl$_2$ to acetone to methanol). Several separate bands were isolated. The product has been isolated as a light
yellow solid which X-ray and molecular weight analyses indicate is triphenylbenzoic acid, a further oxidation product of $\mathcal{V}_{12}$CHO. How this product and other products are formed is unknown at present.

Once isolation of $\mathcal{V}_{12}$CHO was complete, the synthesis of $\text{H}_{2}\text{TPPF}$ was undertaken. Many different systems were experimented with as indicated in table 2.

<table>
<thead>
<tr>
<th>REACTION</th>
<th>CONC. $\mathcal{V}_{12}$CHO (M)</th>
<th>EQ. PYRROLE</th>
<th>PYRROLE FORM</th>
<th>SOLVENT SYSTEM</th>
<th>TEMP.</th>
<th>ADDITION TIME OF PYRROLE</th>
<th>REACTION TIME</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.06</td>
<td>1.25</td>
<td>HET</td>
<td>HCAc</td>
<td>118°C</td>
<td>1 sec.</td>
<td>18 hr</td>
</tr>
<tr>
<td>2</td>
<td>0.12</td>
<td>1.00</td>
<td>HET</td>
<td>BENZENE 1 eq. TFA</td>
<td>80°C</td>
<td>1 sec.</td>
<td>20 hr</td>
</tr>
<tr>
<td>3</td>
<td>0.12</td>
<td>1.00</td>
<td>HET</td>
<td>HCAc</td>
<td>118°C</td>
<td>1 sec.</td>
<td>18 hr</td>
</tr>
<tr>
<td>4</td>
<td>0.12</td>
<td>1.00</td>
<td>HET</td>
<td>HCAc</td>
<td>118°C</td>
<td>1 eq. 1 hr eq 4 hrs later</td>
<td>18 hr</td>
</tr>
<tr>
<td>5</td>
<td>0.15</td>
<td>2.00</td>
<td>HET</td>
<td>HCAc</td>
<td>118°C</td>
<td>1 sec.</td>
<td>15 hr</td>
</tr>
<tr>
<td>6</td>
<td>0.30</td>
<td>1.00</td>
<td>HET</td>
<td>HCAc</td>
<td>118°C</td>
<td>6 hrs.</td>
<td>18 hr</td>
</tr>
<tr>
<td>7</td>
<td>0.15</td>
<td>1.00</td>
<td>25 ml. BENZENE</td>
<td>HCAc</td>
<td>110°C</td>
<td>15 hrs.</td>
<td>16 hr</td>
</tr>
<tr>
<td>8</td>
<td>0.15</td>
<td>1.00</td>
<td>25 ml. BENZENE</td>
<td>HCAc</td>
<td>110°C</td>
<td>1 hr.</td>
<td>1 hr</td>
</tr>
<tr>
<td>9</td>
<td>0.15</td>
<td>1.00</td>
<td>HET</td>
<td>HCAc</td>
<td>124°C</td>
<td>1 hr.</td>
<td>1 hr</td>
</tr>
<tr>
<td>10</td>
<td>0.15</td>
<td>1.50</td>
<td>25 ml. BENZENE</td>
<td>HCAc</td>
<td>112°C</td>
<td>13 hrs.</td>
<td>14 hr</td>
</tr>
<tr>
<td>11</td>
<td>0.15</td>
<td>2.00</td>
<td>HET</td>
<td>HCAc</td>
<td>132°C</td>
<td>1 sec.</td>
<td>24 hr</td>
</tr>
</tbody>
</table>

Table 2
reaction conditions for $\text{H}_{2}\text{TPPF}$ synthesis

As the $\text{H}_{2}\text{TPPF}$ yield of each of these reactions was so small (generally <1%), very little quantitative data was gathered. Instead, many partially purified fractions were combined for
further purification in order to isolate an appreciable amount of product at one time. General trends were noted, however, and the optimal conditions were determined. The optimal concentration of $\varnothing_2$CHO is 0.15 M in glacial acetic acid (HOAc). No dependence on pyrrole concentration is evident, but an excess of 50% is used to account for any self- condensation of the pyrrole. The addition time of the pyrrole is the most important variable to control. This addition should be very slow so that the total addition time can be between 13-15 hrs. To facilitate this, the pyrrole is diluted in 25 mls. of benzene and the benzene/pyrrole solution is added dropwise over the time period. The reaction is somewhat temperature dependent and the optimal temperature is between 110-115°C with the solvent being HOAc. Using the optimal conditions stated, a reaction of 5 grams (15mmole) $\varnothing_2$CHO with 1.65 mls. pyrrole (1.5 equivalents) yields 20 mg. of $\mathrm{H}_2\text{TPP}$. This corresponds to \(\sim 0.5\) yield.

Of interest is reaction #2 in table 2. Following the procedure of Dolphin for the synthesis of $\mathrm{H}_2\text{TPP}$, the $\varnothing_2$CHO was dissolved in benzene. Addition of the pyrrole was next, followed by one equivalent of IPA. Contrary to Dolphin's results, no desired porphyrin was found. This system was then abandoned for the acetic acid system.

The only apparent reason for the poor yield previously mentioned is the effect of steric hindrance that the large (2,4,6-trimethoxy)phenyl groups present at the meso positions. The synthesis of analogous porphyrins via Rothemund condensations of 2,4,6-trimethylbenzaldehyde and 2,4,6-trimethoxy
and triethoxy benzaldehydes have been reported. Badger reports <1% yield of the (2,4,6-trimethyl)phenyl substituted porphyrin and 5% yields of the (2,4,6-alkoxy)phenyl porphyrins have been observed. Presumably, steric effects are the major reason for the poor yields of the mesitylene derivative. The phenyl groups of H₂TIPP are even bulkier than the methyl groups of Badger's system. Hence, yields of <1%, while not desirable, are not unexpected.

Recently conditions have been further optimized to produce a yield of 1% of H₂TIPP with 0.15 \( \text{CHCl}_3 \) in refluxing propionic acid and a slow addition of the pyrrole/benzene mixture.

The electronic spectrum of H₂TIPP is shown in figure 4. Addition of para-toluene sulfonic acid gives the dication spectrum in figure 4 (dashed line). The porphyrin shows absorptions at 660nm, 570nm, 525nm, 360nm, with its Soret at 430nm. The dication spectrum shows the collapse of the bands into a broad band at 670nm, and also shows a red shifted Soret (to 450nm.) and a red shift of the 360nm band to 370nm.

The metallation of H₂TIPP proceeds to near quantitative yields. A spectrum of FeTIPP is shown in figure 2.

Oxidant studies of FeTIPP and further studies on this porphyrin molecule are presently being carried on.
Visible spectrum of $\text{H}_2\text{TPP}$ (solid line) and $(\text{Ru(TPP)})^{2+}$ (dashed line).
FIGURE 6

Visible spectrum of $\text{FeIlII}^{22}$
III. EXPERIMENTAL

General:

Gas chromatography was performed on a Hewlett-Packard model 5370A with digital integrator. A six foot OV-101 column was used at 300°C. \( \text{N}_2 \) was the carrier gas. Visible spectra were obtained on a Hitachi 100-30-A UV-vis spectrophotometer. Nuclear spectral data were obtained with a Varian Associates EM-290 A/B, (90 kHz magnet) spectrometer and chemical shifts are reported in parts per million on the \( \delta \) scale from internal tetramethylsilane. Melting points were taken on a Thomas-Hoover capillary tube melting point apparatus and are uncorrected. Mass spec. analysis was performed on a Varian Mat 731 (low resolution-field desorption) and was performed by J. Carter Cook. Elemental and molecular weight analyses were performed by J. Kemeth and associates.

2,4,6-Triphenylbromobenzene

\[
\text{C}_7\text{H}_9\text{Br} + 3\text{Br}_2 \rightarrow \text{C}_7\text{H}_9\text{Br}_3 + 3\text{HBr}
\]

1) Procedure

In a 1-liter round bottom flask equipped with a stir bar are placed 100g (0.33 moles) \( \text{C}_7\text{H}_9\text{Br} \) (Alrich) and 500 ml. \( \text{CS}_2 \). 40 ml. (0.77 mole) \( \text{Br}_2 \) is added. \( \text{HBr} \) is evolved. The solution is left to stir for 18-20 hrs. Using filtered compressed air, the solution is evaporated to approximately 200 ml. 200 ml. methanol is added and the solution is evaporated again to approximately 200 ml. using a previously heated hot water bath (Note 1). The preceding step is repeated (Note 2). The volume is reduced to approximate 100 ml. total volume and
the solution is cooled and filtered. The solid is washed with four 50 ml portions of ice cold methanol. This yields a light tan solid which is air dried. The solid is recrystallized by dissolving in refluxing CH₂Cl₂. 75 ml hexanes is added and the solution is refluxed until it becomes cloudy. It is then cooled to room temperature and stored in a freezer overnight. The solution is filtered and the solid is washed with ice cold methanol. The yield is 120-125 g (94-98% of the theoretical amount) of white solid melting at 129-130°C (Notes 3, 4).

2) Notes

1) Due to the low flash point of CS₂, no form of electrical heat should be used.

2) These steps remove excess Br₂ and CS₂ and prevent oils. It is best to scrape the solid off the sides of the flask and break up the large pieces in order to remove all Br₂.

3) A second crop (2-3 g) can be obtained by concentration of the mother liquid.

4) Literature M.P. = 129-129°C.²⁴

2,4,6-triphenylbenzaldehyde

\[ \begin{align*}
\begin{array}{c}
\Phi_3CBr \\
(1) n-BuLi \\
(2) \text{LCP} \\
\end{array}
\end{align*} \rightarrow \begin{align*}
\Phi_3CCHO
\end{align*} \]

1) Procedure

A 2-liter 3-neck round bottom flask is equipped with a reflux condenser which is connected to a vacuum/manifold, a dropping funnel, and a stir bar. The third neck is fitted with a stopper. All pieces are clamped or wired together,
The system is evacuated and flushed with Aron three times. Positive Aron pressure is maintained throughout the reaction. 100g (0.26 mole) \( \ell \) is added to the flask and is dissolved in 750 ml. benzene. The solution is brought to reflux. 125 ml. n-hull is added dropwise (Notes 1, 2, 3). The color changes from brown to deep red. After 1½ hours of reflux, the solution is light orange. 70 ml. DMP is added dropwise (Note 3). The solution turns deep brown. It is allowed to cool to room temperature whereupon it can be opened to the atmosphere. An approximately equal volume of saturated NH4Cl is added. The organic layer is separated from the aqueous phase and the aqueous layer is washed with CH2Cl2 until colorless. All organic fractions are combined and are dried over anhydrous 

\[ \text{H}_{2}SO_{4} \]. The solution is filtered and rotavapped to dryness, leaving an orange/brown oil. G.C. analysis under conditions noted earlier:

<table>
<thead>
<tr>
<th>RETENTION TIME</th>
<th>AREA</th>
<th>COMPOUND</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.22</td>
<td>39.3</td>
<td>( \ell )</td>
</tr>
<tr>
<td>5.28</td>
<td>50.5</td>
<td>( \ell )CHC</td>
</tr>
<tr>
<td>7.16</td>
<td>1.2</td>
<td>?</td>
</tr>
<tr>
<td>7.67</td>
<td>2.5</td>
<td>?</td>
</tr>
<tr>
<td>8.85</td>
<td>0.6</td>
<td>?</td>
</tr>
<tr>
<td>10.90</td>
<td>4.4</td>
<td>( \ell )COOH (?)</td>
</tr>
<tr>
<td>12.83</td>
<td>0.7</td>
<td>?</td>
</tr>
<tr>
<td>15.07</td>
<td>0.7</td>
<td>?</td>
</tr>
</tbody>
</table>

**TABLE 2**

Yields from \( \ell \)CHC reaction
The mixture is separated via flash chromatography using TLC grade silica gel without binder and eluting with 20% CH₂Cl₂ in Hexanes. The first band is clear (or may have a slight yellow tinge) and corresponds to 3-JH. 18-20% is isolated (Note 4). The second band has a light yellow color and is the 3-CHO. The weight is 34-38% (39-43% of the theoretical yield.) The melting point of the solid is 130-132°C. Anal. Calcd for C₂₃H₁₈C₅O₆, 90.0%; H, 5.4%. Found: C, 89.14%; H, 5.26%. ¹H NMR: singlet at 9.5 ppm (aldehyde proton), multiplet at 7-7.5 ppm (phenyl protons).

2) Notes

1) The n-BuLi must be added to the dropping funnel under an inert atmosphere as it is flammable upon contact with moist air.

2) 15% excess n-BuLi is used.

3) The addition is exothermic so it must proceed slowly in order to control the reaction.

4) The 3-CHO that is isolated can be rebrominated and used for further 3-CHO syntheses.

**meso-tetrakis(2,4,6-triphenylphenyl)porphyrin**

\[ \text{4 3-CHO + 4 pyrrole} \xrightarrow{\text{HClO}_4} \text{H₂TPFP} \]

1) Procedure

50 ml. glacial acetic acid is heated to 113-115°C in a 100 ml. 3-neck round bottom flask equipped with a reflux condenser, a dropping funnel (Note 1) and a stir bar. The third neck is fitted with a stopper. 1.65 ml. pyrrole is added to 25 ml. benzene and placed in the funnel. 5.0 g (0.015 mole)
\( \text{C}_{3}\text{C}=\text{O} \) is dissolved in the hot acetic acid. The pyrrole/benzene mixture is added slowly (approximately 1 drop/8 sec) to the mixture (Note 2). The addition of the pyrrole/benzene mixture takes between 14-16 hrs. The solution is allowed to reflux an additional hour after the addition is complete. An air stream is blown over the hot solution to evaporate the acetic acid. The remaining mixture is dissolved in approximately 10ml. CH\(_2\)Cl\(_2\). Saturated Na\(_2\)CO\(_3\) is added until neutralized. The layers are separated and the aqueous layer is washed with CH\(_2\)Cl\(_2\) until the CH\(_2\)Cl\(_2\) is colorless. The organic fraction is rotavapped to dryness. The mixture is separated via flash chromatography\(^1\)\(^9\) using TLC grade silica gel without binder and eluting with 20\% CH\(_2\)Cl\(_2\) in Hexanes. A blue and/or pink band elutes first. A green band follows and this is collected and rotavapped to dryness. The green band consists of unreacted \( \text{C}_{3}\text{C}=\text{O} \), the product (H\(_2\)TPPF), and a green material which is a condensation product of three aldehyde and four pyrrole units. This band is further separated via reverse phase flash chromatography using RP-2 (Note 3) and eluting with methanol to remove the \( \text{C}_{3}\text{C}=\text{O} \). The porphyrin is isolated as the next band by eluting with CH\(_2\)Cl\(_2\). H\(_2\)TPPF is a tan/brown product. The visible spectrum shows bands at 660nm., 600nm., 570nm., 370nm., and a strong Soret at 430nm. Addition of p-TsCl produces a dication (H\(_4\)(TPPF))\(^{2+}\) spectrum with bands at 670nm., 450nm., and 370nm. (see figure\(^4\)). Yield is \( < 1\% \) of theoretical amount.

2) Notes

1) A pressure equalizing funnel is not used to prevent
reflux of the acetic acid up the side arm, causing the pyrrole to self-condense. Instead, a dropping funnel with a ground glass joint is placed in the neck of the round bottom. The top of the funnel is closed off with a rubber septum which has a needle through one of the holes to act as a pressure equalizer.

2) The addition rate should be monitored as it tends to drop off due to the inefficient dropper system described in note one. It is periodically necessary to increase the flow a bit in order to keep the rate at approximately 1 drop/3 sec.

3) The procedure for making MD-2 (dimethylsiloxane) follows this writeup.

**Dimethylsiloxane**:

1) Procedure

100g. TLC grade silica gel (particle size 0.032-0.063mm) is placed in a 2-liter round bottom flask equipped with condenser and stir bar. 400ml. pyridine and 400ml. toluene are added. 75ml. dichlorodimethylsiloxane is added slowly with stirring (Note1). The mixture is then refluxed for 5-6 hrs. After cooling to room temperature, the mixture is filtered and washed several times with 200ml. portions of methanol (Note2). The solid is dried overnight in an oven. After cooling to room temperature, it is ready for use.

2) Notes

1) HCl gas is evolved upon addition. An unidentified precipitate (probably polydimethylsiloxane) is also produced which eventually stops the stir bar from turning. Adding the
dichlorodimethylsilane slowly minimizes this solid production.

2) Methanol dissolves the precipitate that forms with the addition of dichlorodimethylsilane. The solid should be washed with enough methanol to ensure that all of the precipitate is removed.

**Iodo-tetrakis(2,4,6-triphenylphenyl)porphyrinatoiron(III)**

\[ \text{H}_2\text{TPPP} + \text{I}_2 + \text{Fe} \left( \text{CC} \right)_5 \xrightarrow{\text{toluene} \; \Delta} \text{FeTPPPFI} \]

1) Procedure\(^{23}\)

To 50ml. toluene in a 100ml. round bottom flask is added 80mg. \( \text{H}_2\text{TPPP} \), 52mg. \( \text{I}_2 \) and 0.6ml. \( \text{Fe} \left( \text{CC} \right)_5 \) is added. (Note 1). The mixture is refluxed for seven hours. Using filtered compressed air, the solution is evaporated to dryness. The residue is dissolved in a minimal amount of \( \text{CH}_2\text{Cl}_2 \) and is separated via flash chromatography\(^{18} \) using TLC grade silica gel and eluting with \( \text{CH}_2\text{Cl}_2 \). The metalloporphyrin is a red/brown band that elutes well after any unreacted \( \text{H}_2\text{TPPP} \) has been eluted. A visible spectrum of \( \text{FeTPPPFI} \) is shown in figure 5. It shows absorptions at 530nm., 525nm., and its Soret at 435nm.\(^{22} \) (Note 2).

2) Notes

1) An excess of \( \text{I}_2 \) and \( \text{Fe} \left( \text{CC} \right)_5 \) is used.

2) This reaction is essentially quantitative (i.e. \( \geq 95\% \) yield).
IV. REFERENCES


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