UNUSUAL METALLOPORPHYRINS. SYNTHESIS AND PROPERTIES OF A DIMETA-ETC(U)

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by

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**Unusual Metalloporphyrins, Synthesis and Properties of a Dimetallic Boron Porphyrin Complex**

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**ABSTRACT:**
Reaction of BCl₃ acetonitrile adduct with tetraphenylporphine affords the corresponding chloro-boron complex. Chromatography of this chelate on alumina results in ligand exchange producing an unusual tetrahydroxydiboron porphyrin. This complex is characterized by visible, IR, NMR, and mass spectrometry, as well as elemental analysis. The diboron derivatives are easily demetalized in solution and are formulated as having out of place structures.
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Abstract: Reaction of BCl₃ acetonitrile adduct with tetraphenylporphine affords the corresponding chloro-boron complex. Chromatography of this chelate on alumina results in ligand exchange producing an unusual tetrahydroxy diboron porphyrin. This complex is characterized by visible, ir, nmr, and mass spectrometry, as well as elemental analysis. The diboron derivatives are easily demetallated in solution and are formulated as having out of plane structures. These may be models for metal ion incorporation into porphyrins.

Introduction: The porphyrin complexes of all the group IIIA elements except boron have been synthesized and well characterized. Although a boron complex of octaethylporphyrin (OEP) has been reported (1964), further work has never subsequently appeared in the commonly available literature and the complex was never well characterized. Such a complex might have interesting medical applications in the treatment of cancer by neutron capture therapy, due to the reported tumor localizing ability of several porphyrins and the high cross section of boron for neutrons. We report here the synthesis and properties of an unusual diboron complex of TPP. A probable structure of the boron porphyrin chelate is also proposed.
Experimental Section:

Physical measurements: Infrared spectra were recorded on a Beckman IR-8 spectrometer as KBr pellets. Mass spectra were obtained on a CEC21-110B mass spectrometer operated at 70 eV. Pmr spectra were recorded in CDCl$_3$ on a Varian HA-100 spectrometer using TMS as an internal standard. C$^{13}$-NMR spectra were obtained on a JEOL PS-100 $^{13}$C pulsed Fourier transfer NMR spectrometer operating at 25 MHz with proton noise decoupling. Spectra were recorded in CDCl$_3$ solution and shifts are reported relative to TMS. Electronic spectra were run on either a Cary-14 or Beckman Model-24 spectrophotometer using 1cm cells.

Reaction of tetraphenylporphine with BCl$_3$: Into a three necked flask were placed 1 ml of reagent grade acetonitrile and 50 ml of dry chlorobenzene. Dry nitrogen was introduced through one neck and exited through a drying tube placed atop a condenser in the center neck. BCl$_3$ was bubbled through an inlet tube in the third neck, with stirring, for about 30 min or until fuming above the inlet occurred. The BCl$_3$·CH$_3$CN adduct precipitated out as a white material. 500 mg of tetraphenylporphine (TPP) was then added and the mixture was brought to reflux. The initially red solution turned green and was allowed to reflux for 24 hrs. After this time the solution had darkened to a reddish green color and the reaction was stopped. The flask was allowed to cool and then kept stoppered at 4°C for three days after which time violet crystals appeared. The product was filtered off, washed with benzene and dried to yield ~ 400 mg of product \( \mathcal{I} \).

Product \( \mathcal{I} \) was not characterized due to its pronounced insolubility and instability in organic solvents. The entire quantity of product \( \mathcal{I} \)
was then chromatographed on basic alumina using benzene and chloroform
as eluants. The benzene elutes off a faint pink fraction that has
been identified as TPP by its visible spectra. The chloroform (which
contains ~1% ethanol to promote ligand exchange) elutes off a deep blue
fraction of the desired product. The solution was evaporated and
dried at reduced pressure to afford an almost quantitative yield
(overall yield 70%) of tetrahydroxyl diboron TPP (I), mp > 350°C.
Calcd. for C_{44}H_{32}N_{4}B_{2}O_{4}·1/2C_{2}H_{5}OH: C, 74.51; H, 5.16; N, 7.26; B, 2.98.
Found: C, 74.70; H, 5.16; N, 7.26; B, 2.97.

\[ \lambda_{\text{max}} \text{(EtOH)} = 427 \text{ nm (117,000)}, 531 \text{ (2,600)}, 573 \text{ (10,100)}, 622 \text{ (10,500)}. \]

PMR(CDC13) 1.05 ppm(m), 3.88(m), 7.78(m), 8.30(m), 8.64(s), 8.96(s)

IR(KBr) 3400 cm\(^{-1}\), 2950, 2890, 1269, 1252, 1093, 1070, 760.

Results and Discussion

PMR: The PMR spectrum is fairly typical of TPP complexes except
that the \( \beta \)-pyrrole protons are split into a doublet. The low intensity
peaks observed at 1.05 and 3.88 ppm have tentatively been assigned to
the methyl and methylene protons respectively of the ethanol of
crystallization. A broad multiplet corresponding to 12 protons at 7.78
ppm represents the meta and para protons of the meso-phenyl groups.
A multiplet at 8.30 ppm corresponds to 8 protons and is assigned to the
ortho phenyl protons. Two sharp singlets at 8.64 and 8.96 ppm (4 protons
apiece) are the \( \beta \)-pyrrole protons on the macrocyclic ring. The ex-
istence of two resonances for the \( \beta \)-pyrrole hydrogens indicates that
the boron is asymmetrically coordinated to the porphyrin ring. Similar
splittings have been observed in the highly asymmetrically coordinated 
H-Re(CO)_3TPP^9 and in TPP itself when the N-H tautomerism is frozen out.\(^{10}\)
In addition the resonances are at abnormally high field values (for 
metal TPP complexes) indicating some distortion of the porphyrin ring. 
Such a distortion would be expected to reduce the ring current and 
cause an upfield shift for \(\beta\)-pyrrole proton resonances. The values found 
are similar to those in the \(\text{H}_4\text{(TPyP)}^{2+}\) and \(\text{H}_4\text{(TPP)}^{2+}\) dications.\(^{11}\)
These are known to have highly distorted porphyrin rings with extensive 
ruffling, and to have the phenyl rings more nearly coplanar with the 
porphyrin macrocycle. Such enhanced coplanarity is expected to 
result in bathochromic shifts in the visible spectra of this compound due to increased resonance interaction between the two ring systems. 
It also may explain why there is no non-equivalence of the \(\alpha\)-phenyl 
protons, as has been observed in many unsymmetrically coordinated 
metalloporphyrins. One final point to note is the failure to observe 
any signals corresponding to the hydroxyl hydrogens. This is not un-
expected and appears to be the rule rather than the exception in 
hydroxy or aquo metalloporphyrins.\(^{12}\)

\(\text{C}^{13}\text{nmr:}\) The \(\text{C}^{13}\) spectrum for compound II was obtained 
Due to relatively poor signal noise ratios and the apparent 
broadening of many of the resonances a completely satisfactory 
spectrum was not obtained and only partial assignments are attempted 
here. Assignments are based on comparison with free TPP and previously 
established metallo-TPP spectra.\(^{13}\) The \(\alpha\)-pyrrole carbon resonances 
are observed as a doublet at 147.8 and 147.0 ppm, indicating two dif-
ferent environments for these carbons. The \(\alpha\)-pyrrole carbons are not
observed in some free base porphyrins but are seen in the metallo-
complexes presumably due to N-H tautomerism in the free base.\textsuperscript{11} The $\beta$-
carbon signals are broadened beyond observation in the boron complex
as no resonance near 132 ppm is seen. We attribute this to B-N tauto-
merism in the metallocomplex with two distinct $\alpha$-carbon sites frozen
out while the $\beta$-carbon resonances are approaching coalescence. A similar
phenomena has been observed in free base and N,N'-dideutero TPP, with an
increasing coalescence temperature for the heavier isotope.\textsuperscript{14} If this
assignment is correct we can then assign a resonance of 142.0 as the
$C_1$ of the phenyl ring and one at 128.2 as the $C_3-C_3'$ carbons. A
peak at 125.9 can be assigned as the $C_4$ phenyl carbon by comparison with
known spectra. A complicated set of broad peaks with maxima at
137.3 and 135.1 ppm must be the $C_2$ and $C_2'$ ortho carbons, which are
apparently non-equivalent. Although we observe no clear non-equivalence
in the H\textsuperscript{1} nmr spectra, the o-hydrogen peak is broad and the shift
differences are expected to be about twice as great in the C\textsuperscript{13} spectra.\textsuperscript{13}
The meso carbon peak is also broadened in the C\textsuperscript{13} spectra but is
assigned at 123.3 ppm. The carbons for the ethanol of crystallization
were not observed.

Visible Absorption Spectra: The electronic absorption spectra of
\textsuperscript{14} is shown in Fig. 1. Complex \textsuperscript{14} gives a normal two banded spectrum and
shows a bathochromatic shift compared to most other metalloporphyrins.
A pronounced metal effect has been observed\textsuperscript{15} in the monometallic group
IIIA OEP complexes. Along this series there is a significant red shift
and a decrease in the Q(0,0)/Q(1,0) intensity ratio. This trend appears
to be reversed for in dimetallic boron complex (\textsuperscript{14}) (no mono boron
complexes are known). The spectra of BB is blue shifted and the Q(0,0)/Q(1,0) ratio is nearly equal to unity, opposite of what would be expected for the mono boron complex. The spectrum is very similar to that of the disodium and dilithium TPP complexes reported by Dorough et al. This may be a consequence of highly ionic metal porphyrin bonds in BB or of an out of plane position for the boron moiety.

**Infrared Spectra:** The IR spectrum of BB shows new bands as indicated in the Experimental section. No strong bands are observed in the region between 1300—1400 cm⁻¹ where normal B—O—B, B—O and B—N stretching modes are found. However, the presence of strong bands at 1003 and 1070 cm⁻¹ and 1269 and 1252 cm⁻¹ can be assigned to the B=N (dative bond) and B—O stretching respectively.¹⁷ The decrease in frequency and intensity of the B—O stretching vibrations indicates no resonance interactions such as

\[
\begin{align*}
R-O^+ & \quad \leftrightarrow \quad R-O^+ \quad \leftrightarrow \quad R-O^+ \\
R' & \quad R' & \quad R'
\end{align*}
\]

are occurring, as the high frequency and intensity in normal boron complexes with unfilled octets have been attributed to such structures.¹⁷ Resonance of this type is largely suppressed when these compounds are coupled to electron donors such as pyridine or other tertiary bases. Thus we conclude that the boron octet is being filled by one of the adjacent nitrogens of the porphyrin ring (as in Fig. 2). This is further supported by the strong bands at ~1100 cm⁻¹ which are indicative of B=N dative bonds. The normal B—N stretching bands may be overlapped with the B—O bands for the same reasons as already outlined.
Finally a broad weak OH band can be seen at about 3400 cm$^{-1}$.

**Mass Spectra:** The use of mass spectra in porphyrin chemistry has been spurred by the usual stability of the molecular ion which is often the base peak facilitating determination of the molecular weight. However, Smith et al. have reported unusual mass spectral patterns for thallium (III) porphyrins where the demetallated ligand is the base peak. In the boron porphyrin the parent molecular ion as m/s 702 is found but is weak (Table 1). We observe that the demetallated ligand is an abundant peak but the doubly charged ion corresponding to $[\text{B}_2\text{OHTPP}]^{2+}$ is the base peak, with other high abundance peaks corresponding to $[\text{B}_2\text{OHTPP}]^{+}$ and $\text{H}_2\text{TPP}^{+}$. Thomas reports a very stable $[\text{B}_2\text{O}\cdot\text{porphyrin}]$ moiety in the mass spectra of the boron-OEP complex.

The fragmentation pattern observed is difficult to explain. The peaks at m/e 687 and 674, presumably reflect loss of axial ligands from boron; however, they do not correspond to any reasonable mass units and may be decomposition peaks. In addition we observe a stable $\text{B}_2\text{OH}$ moiety in the center rather than a $\text{B}_2\text{O}$. Whether the $\text{H}^+$ has been transferred from the axial ligands to the macrocycle or is present as a $\text{H}_2\text{O} \cdot \text{B}^+ \cdot \text{B}^+$ entity is unknown. Such proton transfers are known and in fact two protons must be transferred to the macrocycle to give the $\text{H}_2\text{TPP}^+$ ion. The directly demetallated ligand is also observed.

Demetallation of $\mathbf{I}_5$: Complex $\mathbf{I}_5$ is demetallated slowly in ethanol by water, more rapidly by acetic acid and instantaneously by $\text{HCl/CH}_2\text{C}_2\text{H}_2$. Thus it belongs to stability class V.

Complex $\mathbf{I}_6$ is stable in pure dry methylene chloride but in $\text{CH}_2\text{Cl}_2$ containing a trace of acid the complex goes through a series of transformations with time which yield free TPP or $\text{H}_2\text{TPP}^{2+}$ depending on the quantity
of acid added. These transformations are similar in appearance to those reported by Smith et al. for HgTPP which they ascribe to the following reactions.\(^\text{20}\)

\[
\begin{align*}
2\text{HgTPP} + 2\text{HCl} &\rightarrow \text{TPPH} + \text{Cl-Hg-TPP-Hg-Cl} \\
\text{Cl-Hg-TPP-Hg-Cl} + 2\text{HCl} &\rightarrow \text{TPPH}_2 + 2\text{HgCl}_2
\end{align*}
\]

Fig. 3 shows the transformation with time of \(\lambda\) into other species with \(\lambda_{\text{max}}\) 420 nm and 445 nm. We have identified these two species as \(\text{H}_2\text{TPP}\) and \(\text{H}_4\text{TPP}^{2+}\) by their characteristic visible spectra. An isobestic point is observed at 437 nm. In the presence of slightly more acid, Fig. 4 is obtained where \(\lambda\) has been directly demetallated into \(\text{H}_2\text{TPP}\) without detection of intermediates and is slowly converted into the diacid. A third intermediate (Fig. 5) has also been detected by monitoring the reaction in the visible region (500-700 nm). Prior to formation of \(\text{H}_2\text{TPP}\) an additional species is present, which is identified by its strong absorption at 498 nm, a position where neither \(\text{H}_2\text{TPP}\), \(\text{H}_4\text{TPP}^{2+}\) nor \(\lambda\) absorb. We believe this corresponds to \(\lambda\) the monometallic intermediate. Smith has proposed a dimetallic HgTPP complex as an intermediate in the demetallation of mercury tetraphenylporphine which decomposes to give a monochloro monomercury TPP derivative and ultimately to yield \(\text{H}_2\text{TPP}\). Our results indicate a similar process, starting with the dimetallic boron complex. The demetallation of metal porphyrins is thought to proceed via protonation of the complex followed by loss of metal ion from the back side of the molecule.\(^\text{21}\) Thus we may postulate a tentative mechanism for the demetallation of \(\lambda\).
Thus the demetallation in acid proceeds through free H$_2$TPP and thence to the diacid. In very weakly acidic solutions an additional intermediate \( \text{III} \) can be detected. This is further evidence for the dimetallic intermediate proposed as models for metal ion insertion into porphyrins and is consistent with Smith's model for the demetallation of HgTPP.

**Proposed Structure:** Due to the protracted difficulties in obtaining a single crystal suitable for x-ray diffraction analysis, we feel justified in proposing a structure for \( \text{II} \) based on the extensive chemical and spectroscopic data. It is difficult to assign an exact structure but the nmr, mass spectra, and infrared analysis are consistent with a structure such as A or B. However, we cannot at this time rule out the alternative structures with absolute certainty.

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References

1) University Health Fellow.


8) If highly dried and purified CHCl₃ (ethanol preservative removed) is used for the chromatography no product is found to elute until some ethanol is added. In addition the product II is unstable in pure CHCl₃ and decomposes rapidly unless ethanol is present. This data in addition to the elemental analysis and nmr lead us to propose ½ mole of ethanol of crystallization.


**TABLE 1**

Relative Intensities of Ion Species of Interest

in the Mass Spectrum of $\Xi_{\alpha \beta}$

<table>
<thead>
<tr>
<th>m/e</th>
<th>rel. abun.</th>
<th>assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>702</td>
<td>6</td>
<td>$M^+$</td>
</tr>
<tr>
<td>687</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>674</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>651</td>
<td>96</td>
<td>$M^+-3OH$</td>
</tr>
<tr>
<td>652</td>
<td>3</td>
<td>$TPP^+$</td>
</tr>
<tr>
<td>325.5</td>
<td>100</td>
<td>$</td>
</tr>
<tr>
<td>307</td>
<td>32</td>
<td></td>
</tr>
</tbody>
</table>

**Isotope peaks of parent ion**

<table>
<thead>
<tr>
<th>m</th>
<th>rel. abun.</th>
</tr>
</thead>
<tbody>
<tr>
<td>m-2</td>
<td>.36</td>
</tr>
<tr>
<td>m-1</td>
<td>.77</td>
</tr>
<tr>
<td>m</td>
<td>1.00</td>
</tr>
<tr>
<td>m+1</td>
<td>.44</td>
</tr>
<tr>
<td>m+2</td>
<td>.13</td>
</tr>
</tbody>
</table>

$m = \text{ion containing the most abundant isotopes of all elements present}$

(assumed $B^{11} \sim 80\%, B^{10} \sim 20\%$)
Figure Captions

Fig. 1. Visible absorption spectrum of compound II in ethanol. Concentration C is 5.4x10^{-5} M.

Fig. 2. Possible structures for compound II. Structure (C) represents the structure proposed by Thomas for the OEP boron complex.

Fig. 3. Repeated traces with time of the Soret region of the electronic absorption spectrum of complex II in CH₂Cl₂ containing a trace of hydrogen chloride.

Fig. 4. Repeated traces with time of the Soret region of the electronic absorption spectrum of complex II in CH₂Cl₂ containing a slightly larger amount of hydrogen chloride (see text).

Fig. 5. Repeated traces with time of the visible absorption spectra of complex II in CH₂Cl₂ containing a trace of hydrogen chloride.
Fig. 1
Fig. 2

(A) 

(B) 

(C)

Fig. 2