

Reactivity of Iron Verdohemes with Phenylmagnesium Bromide. Formation of Paramagnetic Iron–Phenyl Complexes

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Iron(III) porphyrins with phenyl groups as axial ligands are paramagnetic intermediates formed during heme degradation by aryl hydrazines.¹ The corresponding model complexes such as PhFe^{III}(TPP) (TTP is the dianion of *meso*-tetraphenylporphyrin) can be prepared by the reaction of a Grignard reagent with ClFe^{III}(TTP),^{2,3} and one such complex has been characterized crystallographically.⁴ PhFe^{III}(TPP) is a low-spin ($S = 1/2$), five-coordinate complex that reacts in solution with dioxygen to form the corresponding phenoxy complex, PhOFe^{III}(TPP).⁵

Verdohemes are iron complexes of 5-oxaporphyrin, a macrocycle in which an oxygen atom replaces one *meso*-CH group of a porphyrin.⁶ The reaction of the verdoheme Br₂Fe^{III}(OEOP) (See Chart 1) with Grignard reagents has the potential of forming a novel six-coordinate iron(III) complex with two axial aryl groups, if the reactivity of Br₂-Fe^{III}(OEOP) follows that of ClFe^{III}(TTP) and other iron(III) porphyrins. As precedents, it is known that treatment of Br₂-Ni^{II}(O₂TPP) (where O₂TPP is 21,23-dioxaporphyrin) with phenylmagnesium bromide yields paramagnetic Ph₂Ni^{II}(O₂-TPP),⁷ and that both *cis* and *trans* isomers of diamagnetic Ph₂Sn^{II}(TPP) can be isolated.⁸ However, verdohemes are also known to undergo nucleophilic attack on the carbon atoms adjacent to the *meso*-oxygen atom.^{9–11} This process results

in ring opening to form complexes with biliverdin-like ligands. Thus at the outset of this work it was unclear whether a phenyl group could replace an axial halide without attacking the verdoheme macrocycle.

The reactions examined in this study are summarized in Chart 1. Figure 1 shows the ²H NMR spectra that were obtained at 203 K during a titration of a solution of Br₂Fe^{III}(OEOP)⁵ in dichloromethane with a solution of (phenyl-*d*₅)-magnesium bromide in diethyl ether. After the addition of the Grignard reagent, the spectrum shows two resonances in the upfield portion of the spectrum and one in the downfield region. The shifts of these resonances are analogous to the shifts (−111 ppm, *o*-H; −30 ppm, *p*-H; 20 ppm, *m*-H at 223 K) seen for other low-spin Fe(III)–phenyl complexes such as PhFe^{III}(T(*p*-tolyl)P),^{12,13} and the three resonances in this spectrum are ascribed to the formation of PhBrFe^{III}(OEOP). Upon further addition of the (phenyl-*d*₅)-magnesium bromide, the spectrum shown in trace A of Figure 1 disappears, and the spectrum of a new species, designated as [Ph₂Fe(OEOP)]^{•−}, is observed as seen in trace B of Figure 1.⁵ Three paramagnetically shifted resonances due to the phenyl-*d*₅ group are observed, but the pattern of chemical shifts is different from those previously observed for low-spin iron(III) porphyrin complexes that contain a single phenyl ligand.

Figure 2 shows the ¹H NMR spectrum of [Ph₂Fe(OEOP)]^{•−} obtained from the careful addition of phenylmagnesium bromide to a cold (203 K) solution of Br₂Fe^{III}(OEOP).¹⁴ Upon addition of the phenylmagnesium bromide, the resonances of Br₂Fe^{III}(OEOP) are lost and are replaced by the new set of resonances shown in Figure 2. These resonances have been assigned through consideration of their relative integrated

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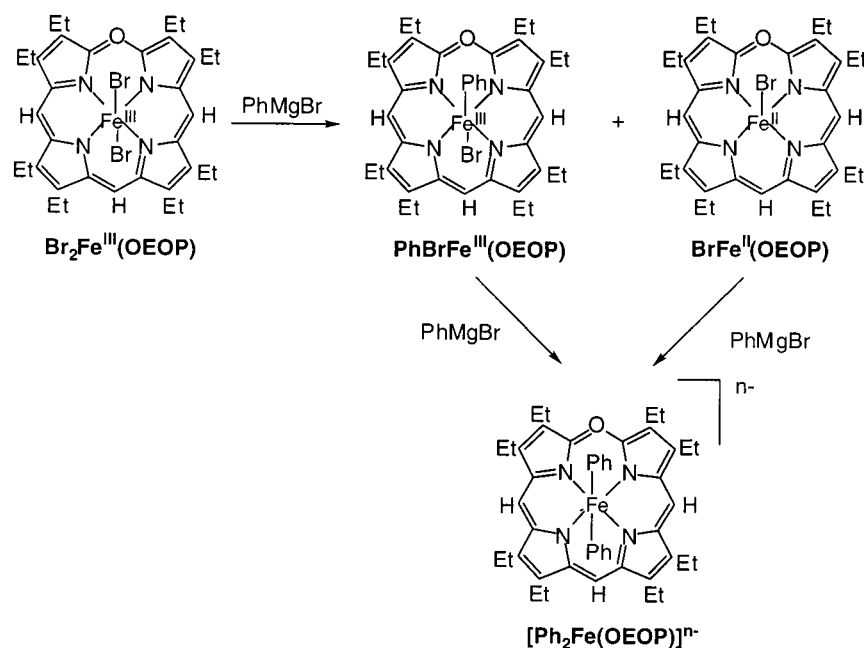
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- (14) Additionally, observation of the ¹H NMR spectra during the early stages of the titration of Br₂Fe^{III}(OEOP) with phenylmagnesium bromide reveals that a significant amount of the reduced verdoheme, BrFe^{II}(OEOP), is formed. The reaction of BrFe^{II}(OEOP) with phenylmagnesium bromide also cleanly produces the intermediate that is responsible for the spectrum shown in trace B of Figure 2 without the formation of other products.

Chart 1



intensities and comparison with spectra of specifically deuterated samples. Thus, the three phenyl resonances are readily assigned by comparison of the data in Figure 2 and trace B of Figure 1. The methyl and methylene resonances of the new intermediate are expanded in trace B'' of Figure 2. There are four methyl resonances (labeled 1*–4*) with equal integrated areas and only four methylene resonances (labeled 1–4) with equal integrated areas. The ratio of the relative integrated intensities of methyl to methylene resonances is 3:2. This pattern of resonances indicates that the axial ligation is equivalent on both sides of the porphyrin plane and is entirely consistent with the formation as $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$. Only a single meso resonance (at -10.2 ppm) is observed in the ^1H NMR spectrum shown in Figure 2. In order to verify the assignment of this resonance and to detect any others, the NMR spectrum of $[\text{Ph}_2\text{Fe}(\text{OEOP-}i\text{meso-}$

$d_3)]^{n-}$ was obtained. That spectrum revealed the presence of two meso resonances, one that corresponds to the

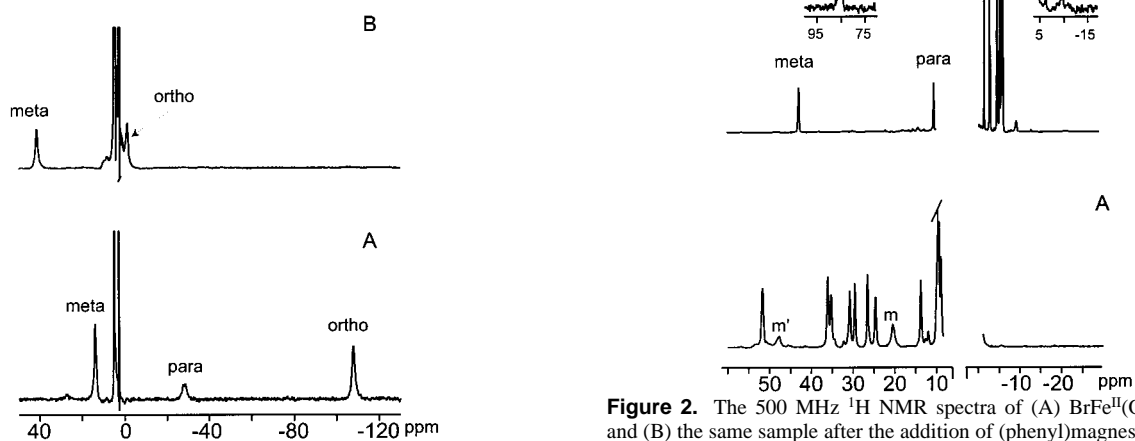


Figure 1. The 76.77 MHz ^2H NMR spectra of a 3 mM solution of $\text{Br}_2\text{Fe}^{\text{III}}(\text{OEOP})$ in dichloromethane at 203 K after the addition of a solution of (phenyl- d_5)magnesium bromide in diethyl ether. The data in trace A were collected in the early stages of addition (0.25 equiv) where $\text{PhBrFe}^{\text{III}}(\text{OEOP})$ formed while the spectrum of $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ in trace B resulted from the addition of further (phenyl- d_5)magnesium bromide (1 equiv). The ortho, meta, and para phenyl resonances are labeled ortho, meta, and para, respectively.

Figure 2. The 500 MHz ^1H NMR spectra of (A) $\text{BrFe}^{\text{II}}(\text{OEOP})$ alone and (B) the same sample after the addition of (phenyl)magnesium bromide in diethyl ether to form $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ at 203 K. Inset B' shows resonances in the 76.77 MHz ^2H NMR spectrum of a 3 mM solution of $\text{BrFe}^{\text{II}}(\text{OEOP-}i\text{meso-}d_3)$ after the addition of (phenyl)magnesium bromide in diethyl ether at 203 K. Trace B'' shows an expansion of the upfield region of the spectrum shown in trace B. Methyl resonances are labeled 1*–4*, methylene resonances are labeled 1–4, meso resonances are labeled m and m', and the ortho, meta, and para phenyl resonances are labeled ortho, meta and para, respectively.

previously detected meso resonance at -10.2 ppm and another resonance in the far downfield region at 85 ppm as seen in trace B' of Figure 2. A plot of the chemical shifts of the ^1H NMR resonances of $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ versus $1/T$ is linear within the short temperature range (from 203 to 240 K) over which we could observe this species.

The acquisition of an MCOASY spectrum for $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ has allowed the methylene and methyl resonances of the four individual ethyl groups of the intermediate to be paired.¹⁵ Thus, cross peaks are observed between the methylene resonance labeled 1 and the methyl resonance labeled 1*. Likewise there are cross peaks connecting methylene resonance 2* and methyl resonance 2 and so on. In addition there is a strong cross peak between the phenyl p -H at 11 ppm and the downfield phenyl resonance at 43 ppm. Thus, the downfield phenyl resonance at 43 ppm is assigned to the meta protons of the phenyl ligands.

The pattern of resonances seen in Figures 1 and 2 is consistent with the formulation of $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ as shown in Chart 1. Consideration of the integrated intensities of the phenyl resonances and the integrated intensities of the methyl and methylene resonances indicates that there are two phenyl groups axially bound to the iron 5-oxaporphyrin. To confirm this point and to verify the assignment of the para phenyl proton in the spectrum shown in Figure 2, spectra were obtained from samples prepared by adding p -tolylmagnesium bromide and a mixture of p -tolylmagnesium bromide and phenylmagnesium bromide to $\text{Br}_2\text{Fe}^{\text{III}}(\text{OEOP})$. The results are shown in Figure 3. Trace A shows the downfield region of the spectrum of $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ while trace C shows the corresponding portion of the spectrum of $[(p\text{-tolyl})_2\text{Fe}(\text{OEOP})]^{n-}$. The new resonance (intensity, 2×3 protons) seen at 44.2 ppm in trace C is due to protons of the p -methyl group, while the m -H resonance (intensity, 2×2 protons) has shifted to 42.8 ppm. The resonance at 10 ppm due to the para proton of the phenyl ligand in the spectrum shown in Figure 2 is absent from the spectrum of $[(p\text{-tolyl})_2\text{Fe}(\text{OEOP})]^{n-}$. Trace B shows the spectrum obtained by adding a 1:1 mixture of p -tolylmagnesium bromide and phenylmagnesium bromide to $\text{Br}_2\text{Fe}^{\text{III}}(\text{OEOP})$. In addition to the resonances of $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ and $[(p\text{-tolyl})_2\text{Fe}(\text{OEOP})]^{n-}$, there are new resonances due to the formation of the mixed-ligand species, $[\text{Ph}(p\text{-tolyl})\text{Fe}(\text{OEOP})]^{n-}$. These new resonances include a methyl resonance at 45.6 ppm for the p -tolyl group and two m -H resonances (one for the p -tolyl group and one for the phenyl group) at 42.3 and 42.7 ppm.

The newly detected $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ is unstable in solution and requires protection from atmospheric dioxygen. It is also very sensitive to the addition of further quantities of phenylmagnesium bromide. Warming a solution of $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ above 230 K results in the loss of the resonances of this complex in a matter of minutes. The decomposition products have not been identified.

From the spectra shown in Figure 2, it is also clear that the reaction of phenylmagnesium bromide with $\text{Br}_2\text{Fe}^{\text{III}}$ -

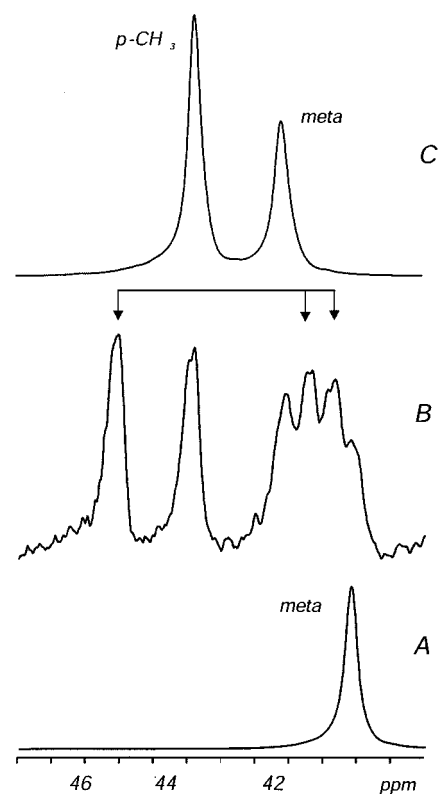


Figure 3. Low-field portions of the 500 MHz ^1H NMR spectra of (A) $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$; (B) a mixture of $[\text{Ph}(p\text{-tolyl})\text{Fe}(\text{OEOP})]^{n-}$, $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$, and $[(p\text{-tolyl})_2\text{Fe}(\text{OEOP})]^{n-}$; and (C) $[(p\text{-tolyl})_2\text{Fe}(\text{OEOP})]^{n-}$ at 203 K. In trace B the arrows show the resonances of the mixed-ligand complex, $[\text{Ph}(p\text{-tolyl})\text{Fe}(\text{OEOP})]^{n-}$.

(OEOP) has not led to addition of the phenyl group to one of the carbon atoms that flank the meso oxygen atom. Addition at that position or addition and ring opening would produce a species whose ^1H NMR spectrum should consist of eight methyl resonances, 16 methylene resonances and three meso resonances as seen in the paramagnetically shifted ^1H NMR spectra that result from the addition of methoxide⁸ or hydroxide¹⁶ to $\text{ClFe}^{\text{II}}(\text{OEOP})$ or $\text{Cl}_2\text{Fe}^{\text{III}}(\text{OEOP})$.

While the spectroscopic properties of the newly detected intermediate are consistent with the $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ stoichiometry, the charge on the complex and the oxidation states of the iron and the verdoheme ligand remain undetermined. Note that $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ can be prepared starting with either $\text{Br}_2\text{Fe}^{\text{III}}(\text{OEOP})$ or $\text{BrFe}^{\text{II}}(\text{OEOP})$, so that redox reactions are clearly a part of the chemistry that occurs here. The formulation of $[\text{Ph}_2\text{Fe}(\text{OEOP})]^{n-}$ as an Fe(II) complex is extremely unlikely. Previous studies in this laboratory have identified a highly reactive iron(II) porphyrin complex with an axial ethyl ligand, $\text{EtFe}^{\text{II}}(\text{TPP})$.¹⁷ That complex is diamagnetic, and we would expect that any monophenyl- or diphenyl-Fe(II) complex, if it formed, would be diamagnetic as well. Additionally, diamagnetic iron(II) phthalocyanine complexes have been prepared with an axial alkyl ligand.¹⁸

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NOTE

However, the intermediate that produces the ^1H NMR spectrum shown in Figure 2 is clearly paramagnetic. The pattern of ^1H and ^2H NMR resonances of this intermediate are unlike those of any other verdoheme complex now known, which include high-spin ($S = 5/2$) and low-spin ($S = 1/2$) Fe(III) and high-spin ($S = 2$) and low-spin ($S = 0$) Fe(II).^{5,19} Of particular significance are the spread of the *meso*-H resonances, one upfield and the other downfield, and the unusual pattern of phenyl resonances which appear to result from a combination of both σ and π spin delocalization pathways. Thus, the observed array of phenyl resonances can be related to the low-spin pattern (*m*-H phenyl resonances shifted downfield, *o*-H and *p*-H resonances shifted upfield) seen for Fe^{III}-Ph compounds, which is then shifted downfield through a strong σ contribution as observed for nickel(II) complexes.⁶ Likewise it is unlikely that Fe(III) is involved, since we definitely observe reduction occurring during the addition of the Grignard reagent and the pattern of ^1H and ^2H NMR resonances does not correspond to any previously observed species. Other possibilities include Fe(I) which is d^7 with $n = 2$ or Fe(0) which is d^8 with $n = 3$. The former, Fe(I), with an $S = 1/2$ ground electronic state, seems the most likely. Related reductions have been observed in the reactions of Grignard reagents with nickel(II) carba-porphyrins²⁰ and in the electrochemical reduction of aryliron porphyrins.³ Also the one-electron reduction of $[(\text{py})_2\text{Fe}^{\text{II}}(\text{OEOP})]^+$ has been observed electrochemically.²¹

The observations reported here also parallel, in part, results obtained from the reaction of phenylmagnesium bromide with ClFe^{III}(OPTAP) (OPTAP is the dianion of tetraazapor-

phyrin), a porphyrin-like complex with four nitrogen atoms replacing the four *meso*-C-H groups. In this case the reaction leads to the formation of a stable, low-spin, iron-phenyl complex, PhFe^{III}(OPTAP).²²

Experimental Section

Preparation of Compounds. The iron complexes Br₂Fe^{III}-(OEOP),⁵ BrFe^{II}(OEOP),⁵ and Br₂Fe^{III}(OEOP-*meso-d*₃)¹⁵ were prepared as described previously.

Phenylmagnesium Bromide Addition to Br₂Fe^{III}(OEOP). Samples for spectroscopic study were prepared in dioxygen-free solvents under dinitrogen atmosphere in a glovebox. Sample concentration for the iron complexes were in the range 1–3 mM. Aliquots of a 1 M solution of phenylmagnesium bromide in diethyl ether (Aldrich) were added at 203 K to a solution of Br₂Fe^{III}(OEOP) or BrFe^{II}(OEOP) in dichloromethane-*d*₂ which was placed in a 5 mm NMR tube and carefully sealed with a septum cap covered with Parafilm. Progress of the reaction was monitored by ^1H NMR spectroscopy.

Instrumentation. ^1H NMR spectra were recorded on a General Electric QE-300 FT NMR spectrometer, a Bruker AMX300 spectrometer, or a Bruker Avance 500 spectrometer operating in the quadrature mode (^1H frequency is 300 MHz for the first two spectrometers and 500 MHz for the last). An exponential window function has been applied to improve the signal-to-noise ratio. The residual ^1H resonances of the deuterated solvents were used as secondary references.

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