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Synthesis and Triiron Complexes of PDK, a New Porphyrin-Linked Dicarboxylate Ligand

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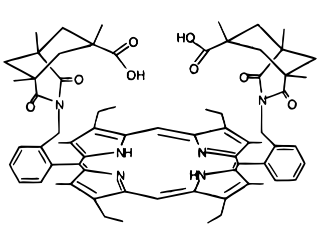
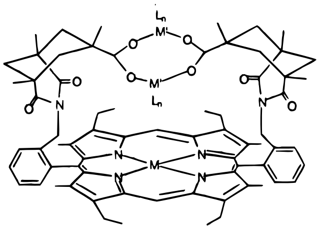
Many challenging chemical transformations are mediated by metalloenzymes having two or more metal ions in close proximity.[1] Carboxylate-bridged diiron centers in soluble methane monooxygenase (sMMO) and ribonucleotide reductase (RNR)[2−4] are two such examples where dioxygen is activated for subsequent hydroxylation and tyrosyl radical generation reactions, respectively. In sMMO, the chemistry is carried out at dinuclear iron centers located within the hydroxylase enzyme, but electrons required for catalytic turnover are supplied by a separate reductase protein.[5] Previously, we reported the use of the convergent dicarboxylate ligand XDK, where H_2XDK is *m*-xylylenediamine bis(Kemp's triacid imide), to assemble carboxylate-bridged diiron complexes that mimic the properties of the sMMO and RNR active sites.[6−8] In the present study, we were interested in designing and preparing a ligand in which the *m*-xylylenediamine linker of XDK was replaced by a metalloporphyrin moiety. Such a construct would have the potential to activate dioxygen and other small molecules within a trimetallic cavity while offering the possibility to supply additional reducing equivalents such as the reductase in the sMMO system. Although complexes in which a metalloporphyrin is linked to a second metal-binding functionality have been of recent interest[9−12] and several porphyrin compounds containing an appended Kemp's triacid[13,14] unit have been synthesized for the purpose of molecular recognition,[15−18] there was no prior example of the kind of trinucleating system we envisioned. Herein we report the efficient synthesis of the desired ligand, designated α,α-PDK for porphyrin-based diaminobis(Kemp's triacid imide), and the preparation, structural characterization, and preliminary reactivity studies of several triiron PDK complexes.



(PDK)H_4



[MM'$_2$L$_n$(PDK)]

The target ligand, α,α-5,15-bis(α-*N*-(Kemp's triacid imido)-*o*-tolyl)-2,8,12,18-tetraethyl-3,7,13,17-tetramethylporphyrin, H_4-(α,α-PDK), was synthesized by first coupling Kemp's triacid anhydride-chloride and a bis(diaminomethyl)phenyl-substituted porphyrin in a manner similar to that employed for preparing H_2-(XDK), Scheme 1.[19,20] The dimeso-substituted octaalkylporphyrin unit **3**, carrying a bromomethyl group at the ortho positions of the two meso-phenyl groups, was obtained from (3,3′-diethyl-4,4′-dimethyl-2,2′-dipyrrolyl)methane (**2**) and α-bromo-*o*-tolualdehyde (**1**). Porphyrins **3**, a mixture of α,α- and α,*β*-atropisomers, were separated by flash column chromatography on silica gel. The structures of both α,α- and α,*β*-isomers, obtained as the zinc complex and free base, respectively, of bromoporphyrin **3** were unambiguously identified by crystallographic chemical analysis (Figures S1−S4, Supporting Information). The α,α-isomer of bromomethyl porphyrin **3** was converted to its aminomethyl derivative **5** through the intermediate imidoporphyrin **4** by Gabriel synthesis. The α,α-bis(aminomethyl)porphyrin **5** was then coupled with Kemp's triacid anhydride-chloride to afford H_4(α,α-PDK) in overall ∼10% yield and gram quantities.

The triiron(II) complex [Fe_3(α,α-PDK)(Lut)(Br)$_2$(HBr)] was obtained in 71% yield by reacting H_4(α,α-PDK) with anhydrous $FeBr_2$ in the presence of 2,6-lutidine in THF at reflux under an inert atmosphere (Scheme 1).[21−23] An X-ray crystal structure determination (Figure 1) revealed that iron had both inserted into the porphyrin and formed the desired carboxylate-bridged dinuclear unit, $\{Fe_2(\mu\text{-}O_2CR)_2\}^{2+}$. The coordination sphere of one iron atom in the latter unit is completed by a terminal halide ion and the nitrogen atom of a 2,6-lutidine ligand. The other nonheme iron atom is coordinated to a bromide ion, Br(1), and to the bromine atom, Br(3), tentatively assigned (see below) to an HBr molecule produced in the reaction and housed in the cavity formed by the three iron atoms. The dimensions of the cavity are defined by the distances Fe(1)···Fe(2) = 5.490(3) Å, Fe(1)···Fe(3) = 4.494(3) Å, and Fe(2)···Fe(3) = 3.744(3) Å. The bromine atom Br(3) also weakly coordinates to the heme iron, Fe(1), expanding its coordination number to 5, and the hydrogen atom H(001) appears to interact with Fe(2), allowing it also to achieve 5-coordination. Steric protection within the cavity is afforded in part by the two methyl carbon atoms of the ligand, C(104) and C(204), which are within van der Waals contact of one another at 3.78 Å (Figure S5). A similar triiron complex [Fe_3(α,α-PDK)(Lut)(I)$_2$(HI)] was obtained when using anhydrous FeI_2 as the iron source. An X-ray crystal structure determination (Figures S6 and S7) revealed essentially the same geometry as in the bromide analogue (Supporting Information).

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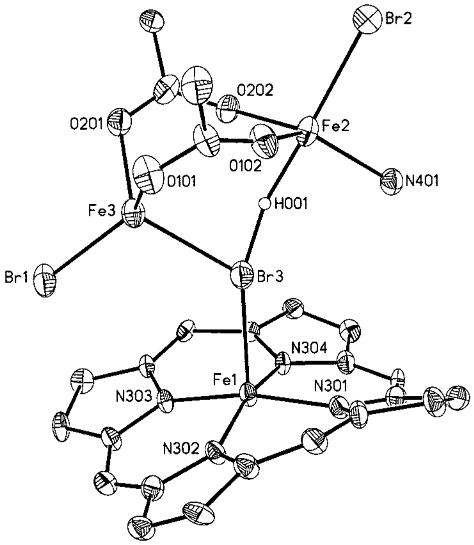
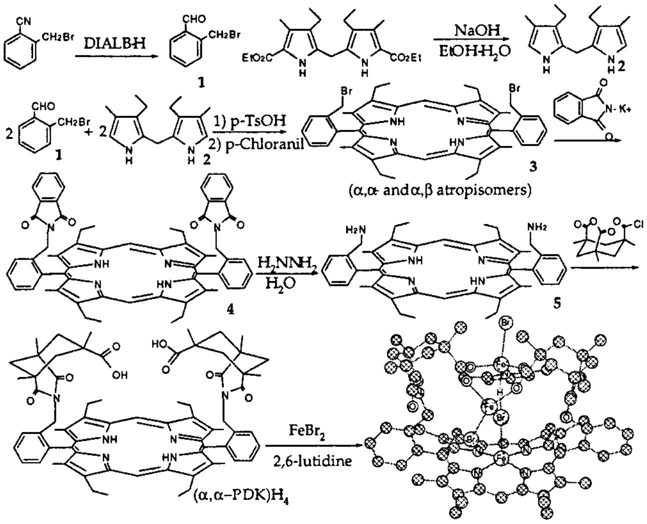


Figure 1. ORTEP showing 30% probability thermal ellipsoids for non-hydrogen atoms of [Fe_3(α,α-PDK)(Lut)$(Br)_2$(HBr)]. For clarity, hydrogen atoms except H(001), the carbon atoms of the coordinated 2,6-lutidine, all of the atoms of α,α-PDK except for the carboxylate group plus the α-carbon atoms and the porphyrin core have been omitted. Selected interatomic distances (Å) and angles (deg): Fe(1)—Br(3), 2.567(2); Fe(2)—N(401), 2.133(10); Fe(2)—O(102), 2.004(9); Fe(2)—O(202), 2.013(9); Fe(2)—Br(2), 2.456(2); Fe(2)—H(001), 1.63(16); Fe(3)—Br(1), 2.366(2); Fe(3)—Br(3), 2.495(2); Fe(3)—O(101), 2.011(9); Fe(3)—O(201), 2.003(8); Br(3)—H(001), 1.50(16); N(401)—Fe(2)—O(102), 128.6(4); N(401)—Fe(2)—O(202), 121.3(4); O(102)—Fe(2)—O(202), 102.4(4); Br(2)—Fe(2)—N(401), 95.3(3); Br(2)—Fe(2)—O(102), 99.0(3); Br(2)—Fe(2)—O(202), 104.2(2); H(001)—Fe(2)—N(401), 89(5); H(001)—Fe(2)—O(102), 75(5); H(001)—Fe(2)—O(202), 79(5); Br(2)—Fe(2)—H(001), 174(5); Br(1)—Fe(3)—Br(3), 106.94(8); Br(1)—Fe(3)—O(101), 130.1(3); Br(1)—Fe(3)—O(201), 104.9(3); Br(3)—Fe(3)—O(101), 102.1(3); Br(3)—Fe(3)—O(201), 119.4(3); O(101)—Fe(3)—O(201), 94.7(4); Br(3)—H(001)—Fe(2), 167(5); Fe(1)—Br(3)—Fe(3), 125.20(8); Fe(1)—Br(3)—H(001), 157(5); Fe(3)—Br(3)—H(001), 77(6). See text for discussion of H(001) identification and placement.

Scheme 1



The presence of a neutral HX molecule in the cavity of the α,α-PDK ligand was unexpected, especially since the reaction was carried out in the presence of excess lutidine added as a base to deprotonate the porphyrin and carboxylic acid functionalities. The assignment of this feature was supported by satisfactory elemental analysis and several additional lines of evidence. The Mössbauer spectrum of solid [Fe_3(α,α-PDK)(Lut)$(Br)_2$(HBr)] displays two overlapping quadrupole doublets with isomer shifts characteristic of three high-spin Fe(II) centers (doublet A: $\delta = 1.08$ mm/s, $\Delta E_Q = 2.05$ mm/s; doublet B: $\delta = 1.09$ mm/s, $\Delta E_Q = 2.48$ mm/s; area ratio: doublet A/doublet B = 2/1; 77 K). These six positive charges are balanced by four negative charges from the tetraanionic PDK ligand and the two terminal bromide ligands. Unless residual electron density in the crystal lattice modeled as pentane is some unidentified cation, an unlikely possibility in view of the analytical data, the central halide ion or some other ligand residue must be protonated. A peak corresponding to H(001) was located between X(3) and Fe(2) in the difference Fourier maps at the position indicated in Figure 1 which behaved well for X = Br when assigned as a hydrogen atom in subsequent least-squares refinements of the structure. This result alone is insufficient to support its location, however, since alternative sites could not be excluded. Accurate positioning and identification of the H atom will have to await the results of a more definitive neutron diffraction analysis, if large enough crystals can be grown.

A series of related, trinuclear PDK complexes, [M_3(α,α-PDK)(μ_i-X)$(L1)_m(L2)_n]^{+j}$, M = Mn, Fe, Co, Ni, Cu, and/or Zn; X = Br, Cl, or F; L1, L2 = Lut, py, THF, H_2O, and/or OTf^-; $i = 2$ or 3; $m = 1$ or 2; $n = 1$ or 2; $j = 0$ or 1), have also been prepared and structurally characterized. They too have metals inserted into the porphyrin and contain the desired carboxylate-bridged dinuclear unit, $\{M_2(\mu\text{-}O_2CR)_2\}^{2+}$. Preliminary studies reveal that [Fe_3(α,α-PDK)(Lut)$(Br)_2$(HBr)] reacts with O_2, CO, and NO, and these reactions are currently under investigation.

In conclusion, the complexes [Fe_3(α,α-PDK)(Lut)$(X)_2$(HX)] (X = Br or I) represent the first examples of triiron species which bring together features of both heme iron and carboxylate-bridged non-heme diiron metalloenzyme cores in a single entity.[11] They offer the possibility of comparing directly the reactivity of these two major types of biological iron and of achieving new chemistry not available for either center in isolation. The proposed binding mode of the HX molecule has implications for several areas of current interest, including transition-state theory, small molecule activation, and hydrogen bonding in organometallic systems.[24-27] The nonplanar conformational distortion of the porphyrin core caused by formation of the carboxylate-bridged diiron unit $\{Fe_2(\mu\text{-}O_2CR)_2\}^{2+}$ and other chemical and structural details will be discussed in more detail elsewhere.[20]

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Supporting Information Available: Synthetic and X-ray structural details for all compounds (71 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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