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## A C<sub>2</sub>-Symmetric, Basic Fe(III) Carboxylate Complex Derived from a Novel Triptycene-Based Chelating Carboxylate Ligand

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### Abstract

A triptycene-based bis(benzoxazole) diacid ligand H<sub>2</sub>L<sup>Ph4</sup> bearing sterically encumbering groups was synthesized. Treatment of H<sub>2</sub>L<sup>Ph4</sup> with Fe(OTf)<sub>3</sub> afforded a C<sub>2</sub>-symmetric trinuclear iron(III) complex, [NaFe<sub>3</sub>(L<sup>Ph4</sup>)<sub>2</sub>(μ<sub>3</sub>-O)(μ-O<sub>2</sub>CCPh<sub>3</sub>)<sub>2</sub>(H<sub>2</sub>O)<sub>3</sub>](OTf)<sub>2</sub> (**8**). The triiron core of this complex adopts the well known “basic iron acetate” structure where the heteroleptic carboxylates, comprising two dianionic ligands (L<sup>Ph4</sup>)<sup>2-</sup> and two Ph<sub>3</sub>CCO<sub>2</sub><sup>-</sup>, donate the six carboxylate bridges. The (L<sup>Ph4</sup>)<sup>2-</sup> ligand undergoes only minor conformational changes upon formation of the complex.

The chemical and physical properties of oxo-bridged triiron carboxylates, also known as “basic iron acetates” (Figure 1), were studied decades ago, and the trinuclear μ<sub>3</sub>-oxo structural motif is recognized as a ubiquitous feature of iron carboxylate chemistry.<sup>1</sup> The widespread occurrence of the {Fe<sub>3</sub>O(O<sub>2</sub>CR)<sub>6</sub>}<sup>+/0</sup> motif is most likely a consequence of its thermodynamic stability, and the unit has been employed as a useful building block of metal-organic frameworks (MOFs) and other solid state materials.<sup>2–5</sup> In addition, this family of complexes displays interesting catalytic properties in olefin epoxidation<sup>6</sup> and the oxidation of C–H bonds.<sup>7,8</sup> Aside from its distinctive {Fe<sub>3</sub>O(O<sub>2</sub>CR)<sub>6</sub>}<sup>+/0</sup> core, several other features are characteristic of basic iron carboxylates. Most such complexes are bridged by ligands derived from six monocarboxylate ligands (Figure 1). The use of chelating diacetate ligands in the core has only recently been reported.<sup>8</sup> Moreover, to our knowledge, basic iron acetates are all derived from a homoleptic set of carboxylate bridges. No {Fe<sub>3</sub>O(O<sub>2</sub>CR)<sub>6</sub>}<sup>+/0</sup> cores bearing a mixture of different carboxylate bridges are known. Here, we describe a novel chiral C<sub>2</sub>-symmetric complex having a triiron(III) basic carboxylate structure that extends the type of known compounds in this class. This cluster contains a chelating dicarboxylate ligand with a triptycene backbone. We report the synthesis, structure, and characterization of the ligand, as well as the triiron(III) complex.

In line with the long-term goal of our laboratory to prepare biomimetic models of the diiron active site of soluble methane monooxygenase hydroxylase (sMMOH) and related bacterial monooxygenases (BMMs),<sup>9–12</sup> we previously synthesized a triptycene-based diester ligand **L1** and studied its iron complexes (Figure 2).<sup>13</sup> To better match the active sites of the BMMs, it is desirable to replace the ester ligands of **L1** with more biologically relevant carboxylate groups, such as those present in the related ligand **H<sub>2</sub>L2**. Although **H<sub>2</sub>L2** can be prepared by hydrolysis of **L1**, subsequent attempts to access iron complexes of this ligand

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<sup>†</sup>Electronic Supplementary Information (ESI) available: Detailed experimental procedures, compound characterization, and the results of <sup>1</sup>H and <sup>13</sup>C NMR spectroscopic and single crystal X-ray diffraction studies. The CSD numbers for compounds **2**, **H<sub>2</sub>L<sup>Ph4</sup>** and complex **8** are CCDC 881380, CCDC 881378, and CCDC 881379, respectively. See DOI: 10.1039/b000000x/

afforded only intractable materials. We hypothesize that the bridging coordination mode of carboxylate ligands<sup>14</sup> may facilitate the formation of insoluble coordination polymers in the case of **H<sub>2</sub>L2**. Inspired by the success imparted by sterically encumbering carboxylate ligands to prevent such polymerization reactions and produce the desired diiron cores,<sup>10,15</sup> we designed a modified version of the ligand, **H<sub>2</sub>L2<sup>Ph4</sup>**, with bulky phenyl groups incorporated at the *ortho* positions of each carboxylic acid in **H<sub>2</sub>L2**. For synthetic convenience, the *para* positions of the carboxylate arenes were also similarly functionalized.

Our proposed synthetic pathway to **H<sub>2</sub>L2<sup>Ph4</sup>** used the diphenyl substituted methyl (3-hydroxy)anthranilate analog **6** as the starting material. The synthesis of **6** commenced with 3-chloro-2-nitrobenzoic acid (Scheme 1). Hydroxylation of this electron deficient chlorobenzene gave 3-hydroxy-2-nitrobenzoic acid (**1**) in quantitative yield. Although dibromination of **1** using Br<sub>2</sub>/HOAc has been reported,<sup>16</sup> we found the conditions to be too harsh, for they produced many side products. An improved reaction condition (Br<sub>2</sub>/NaOAc in EtOH) was devised that was sufficiently mild, affording 4,6-dibromo-3-hydroxy-2-nitrobenzoic acid (**2**) in 71% yield. An X-ray crystal structure of **2** confirmed the desired positions of the two bromine atoms (Figure S2). A two-step, one-pot protection reaction of both the carboxylic acid and the phenol of **2** using diazomethane and dimethylsulfate/K<sub>2</sub>CO<sub>3</sub>, respectively, gave methyl 4,6-dibromo-3-methoxy-2-nitrobenzoate (**3**) in 92% overall yield. Suzuki coupling reaction of **3** with phenyl boronic acid successfully introduced two phenyl groups on both the *ortho* and *para* positions of the arene in **3**, giving **4** in 89% yield. The selective deprotection of the methyl phenyl ether in the presence of the methyl ester in **4** proved challenging. Ester groups are more vulnerable than ethers to deprotection under most commonly used conditions. A literature search revealed that deprotection of nitro-substituted methyl phenol ethers can be accomplished using LiCl as a mild reagent in refluxing DMF.<sup>17</sup> Using this condition, however, resulted in demethylation of the ester moiety. We hypothesized that the high temperature (160 °C) employed might lead to the undesired hydrolysis of the ester group. Therefore, we carried out the reaction with **4** using a lower temperature (90 °C), and only the methyl phenyl ether moiety of **4** was deprotected by LiCl, leaving the ester group unmodified. After purification, phenol **5** was obtained in 86% yield. Finally, methyl anthranilate **6** was achieved in 96% yield after hydrogenation of **5**.

With our desired methyl anthranilate **6** in hand, we moved forward with the assembly of the triptycene backbone. As shown in Scheme 2, amide coupling of **6** with in situ generated benzoyl chloride **i** gave diamide **7** in 70% yield.<sup>13</sup> Next, compound **7** was cyclized using *p*-TsOH·H<sub>2</sub>O in HOAc to give **L1<sup>Ph4</sup>** in 98% yield. Finally, the methyl esters in **L1<sup>Ph4</sup>** were successfully hydrolyzed by BBr<sub>3</sub>, giving **H<sub>2</sub>L2<sup>Ph4</sup>** in 98% yield. The overall yield of this 9-step synthesis is 32%.

X-ray diffraction quality crystals of **H<sub>2</sub>L2<sup>Ph4</sup>** were obtained by slow evaporation of a CD<sub>2</sub>Cl<sub>2</sub> solution in an NMR tube. As shown in Figure 3, the two carboxylic acids in the crystal structure of **H<sub>2</sub>L2<sup>Ph4</sup>** are oriented toward one another. The distances between two pairs of oxygen atoms are 2.676(3) Å and 2.734(3) Å, which are within hydrogen bonding distance. Furthermore, the two hydrogen atoms could be located on the difference Fourier map. The hydrogen bonds orient all of the potential donor atoms toward the center of the ligand. The distance between two nitrogen atoms is 6.013 Å and that between two furan oxygen atoms on the triptycene backbone is 4.780 Å, indicating that the ligand framework will provide a suitable binding pocket for two metal atoms. In addition, the phenyl groups of **H<sub>2</sub>L2<sup>Ph4</sup>** significantly enhance the solubility of this diacid relative to the underivatized analog **H<sub>2</sub>L2** in various non-polar organic solvents; the additional phenyl groups will efficiently increase the hydrophobicity of the ligand.

Treatment of  $\text{H}_2\text{L2}^{\text{Ph4}}$  with  $\text{Fe}(\text{OTf})_3$  and triethylamine in the presence of sodium 2,2,2-triphenylacetate ( $\text{Ph}_3\text{CCO}_2\text{Na}$ ) afforded red crystalline blocks after vapor diffusion of pentane into a benzene solution of the reaction mixture. Although these crystals diffracted only to 1 Å resolution, the structure solution and refinement determined unambiguously the geometry of the complex. The complex is best formulated as  $[\text{NaFe}_3(\text{L2}^{\text{Ph4}})_2(\mu_3\text{-O})(\mu\text{-O}_2\text{CPh}_3)_2(\text{H}_2\text{O})_3](\text{OTf})_2$  (**8**) (Figure 4), and the core is depicted in Figure 5. This latter features a triiron center, bridged internally by a  $\mu_3$ -oxo atom and externally by the carboxylates of  $(\text{L2}^{\text{Ph4}})^{2-}$  and by  $\text{Ph}_3\text{CCO}_2^-$ . Complex **8** has a crystallographically required  $C_2$ -axis passing through the  $\mu_3$ -oxo ion (O12), Fe2 atom, and a coordinated water molecule (O13) (Figure 5). A sodium ion (yellow, Figure 4) forms an intimate ion-pair complex through coordination to carboxylate, water, and benzofuran oxygen atoms of the core structure. The sodium ion is spatially disordered, with 50% occupancy, between the site in the asymmetric unit (Figure 4) and its symmetry generated crystallographic partner (not shown).

The core structure of **8** is shown in Figure 5 (see Figure S5 for detailed information). Among the six carboxylate bridges, four are derived from two  $(\text{L2}^{\text{Ph4}})^{2-}$  anions and the other two are  $\text{Ph}_3\text{CCO}_2^-$ . Although a number of triiron basic carboxylate structures are known, the structure of **8** is unique for several reasons. The use of chelating dicarboxylate ligands for the assembly of this  $\{\text{Fe}_3\text{O}\}^{7+}$  core is rare. Furthermore, to the best of our knowledge, all currently known complexes with such a  $\{\text{Fe}_3\text{O}\}^{7+}$  core are bridged by a homoleptic set of carboxylate ligands. Here, two chemically different carboxylates,  $(\text{L2}^{\text{Ph4}})^{2-}$  and  $\text{Ph}_3\text{CCO}_2^-$ , bridge the iron atoms. Lastly, the large chelate span of  $(\text{L2}^{\text{Ph4}})^{2-}$  gives rise to a chiral structure. Because the complex crystallized in a centrosymmetric space group, both enantiomers are present. Another noteworthy feature of this structure is the apparent lack of coordination of the benzoxazole nitrogen atoms. We hypothesize that the low basicity of benzoxazole renders such coordination unfavorable.

Mössbauer spectroscopy was performed to verify the oxidation state assignment of the Fe atoms. The zero-field  $^{57}\text{Fe}$  Mössbauer spectrum at 77 K, together with the fit, are shown in Figure S1 and Table 1, respectively. The data were best fit with a two-site model. The approximate ratio of the two iron sites was 2:1, consistent with the presence of two chemically inequivalent Fe sites observed in the X-ray structure. The major site has an isomer shift of ( $\delta$ ) 0.472 mm/s and quadrupole splitting of ( $\Delta E_q$ ) 0.604 mm/s. The minor site has an isomer shift of ( $\delta$ ) 0.684 mm/s and quadrupole splitting of ( $\Delta E_q$ ) 0.600 mm/s. These values are consistent with those of other triiron(III) centers having a basic carboxylate structural motif.<sup>8,18</sup>

## Conclusions

In summary, we describe the synthesis of a preorganized triptycene-based bis(benzoxazole) ligand,  $\text{H}_2\text{L2}^{\text{Ph4}}$ . To prevent undesired formation of high nuclearity clusters and polymers, sterically protecting phenyl groups were installed *ortho* to the carboxylic acid units in the  $\text{H}_2\text{L2}^{\text{Ph4}}$  ligand. A triiron(III) complex  $[\text{NaFe}_3(\text{L2}^{\text{Ph4}})_2(\mu_3\text{-O})(\mu\text{-O}_2\text{CCPh}_3)_2(\text{H}_2\text{O})_3](\text{OTf})_2$  (**8**), was obtained having a “basic iron acetate” core in the structure. Among this class of compounds, the structure of **8** is novel because it utilizes a chelating dicarboxylate ligand, is constructed from two different types of carboxylate bridges, and is chiral. The observation that the benzoxazole nitrogen fails to coordinate to iron suggests that a more basic *N*-donor is needed to successfully model the diiron site of sMMOH. The design and synthesis of more basic analogs of  $\text{H}_2\text{L2}^{\text{Ph4}}$  is the focus of our ongoing work.

## Supplementary Material

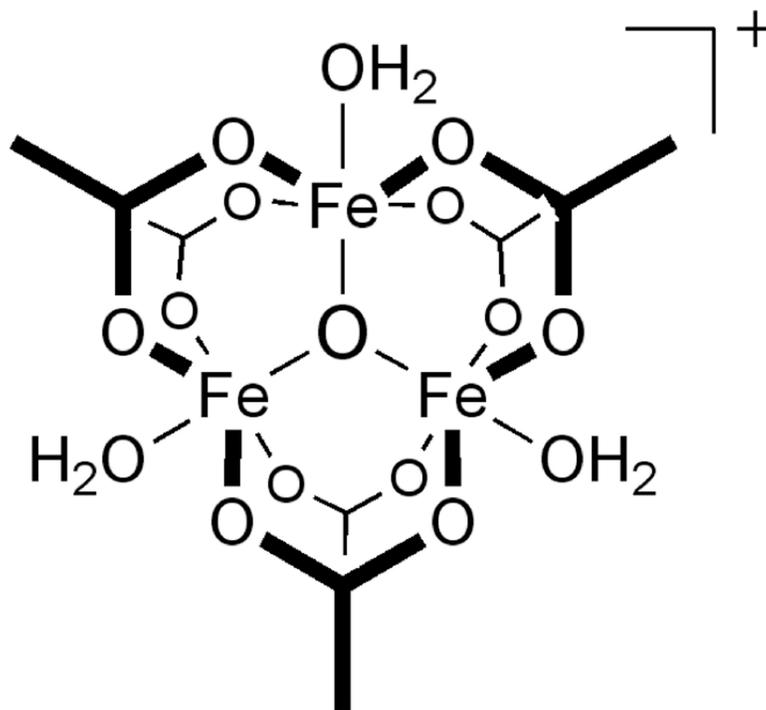
Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

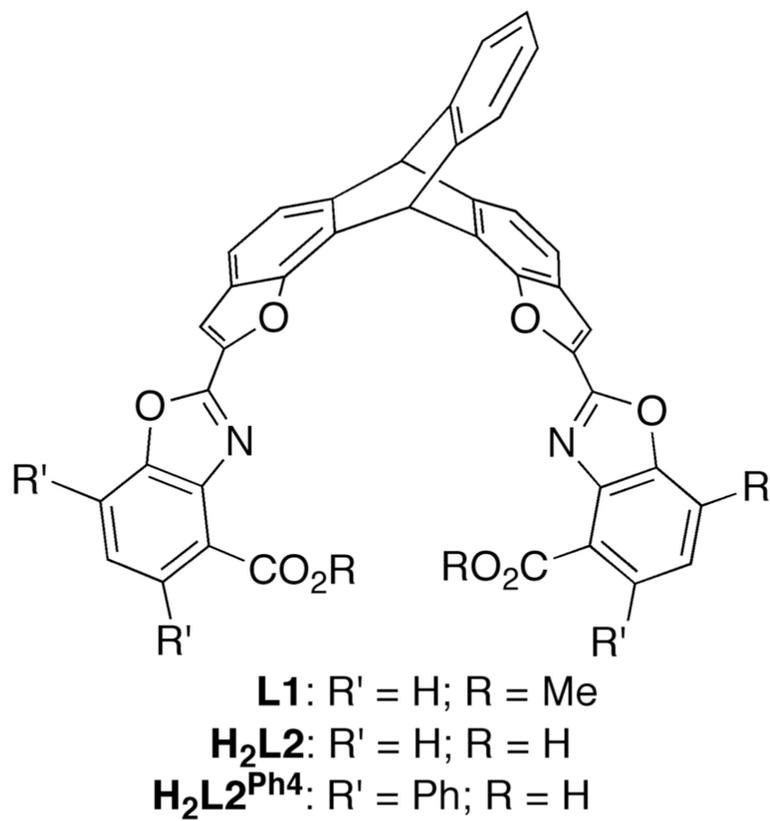
This work was supported by a grant from the National Institute of General Medical Sciences. Dr. Apfel thanks the Alexander von Humboldt Foundation and a Feodor Lynen research fellowship.

## Notes and references

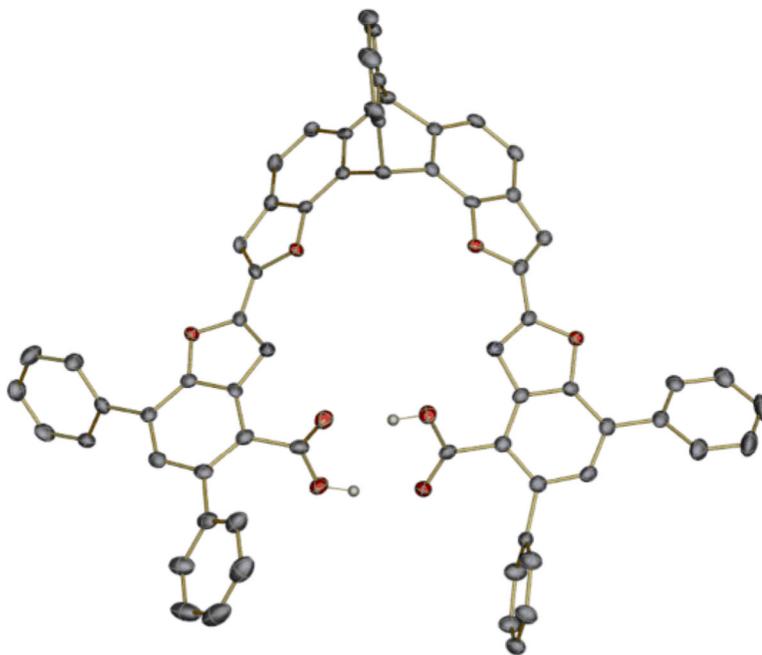
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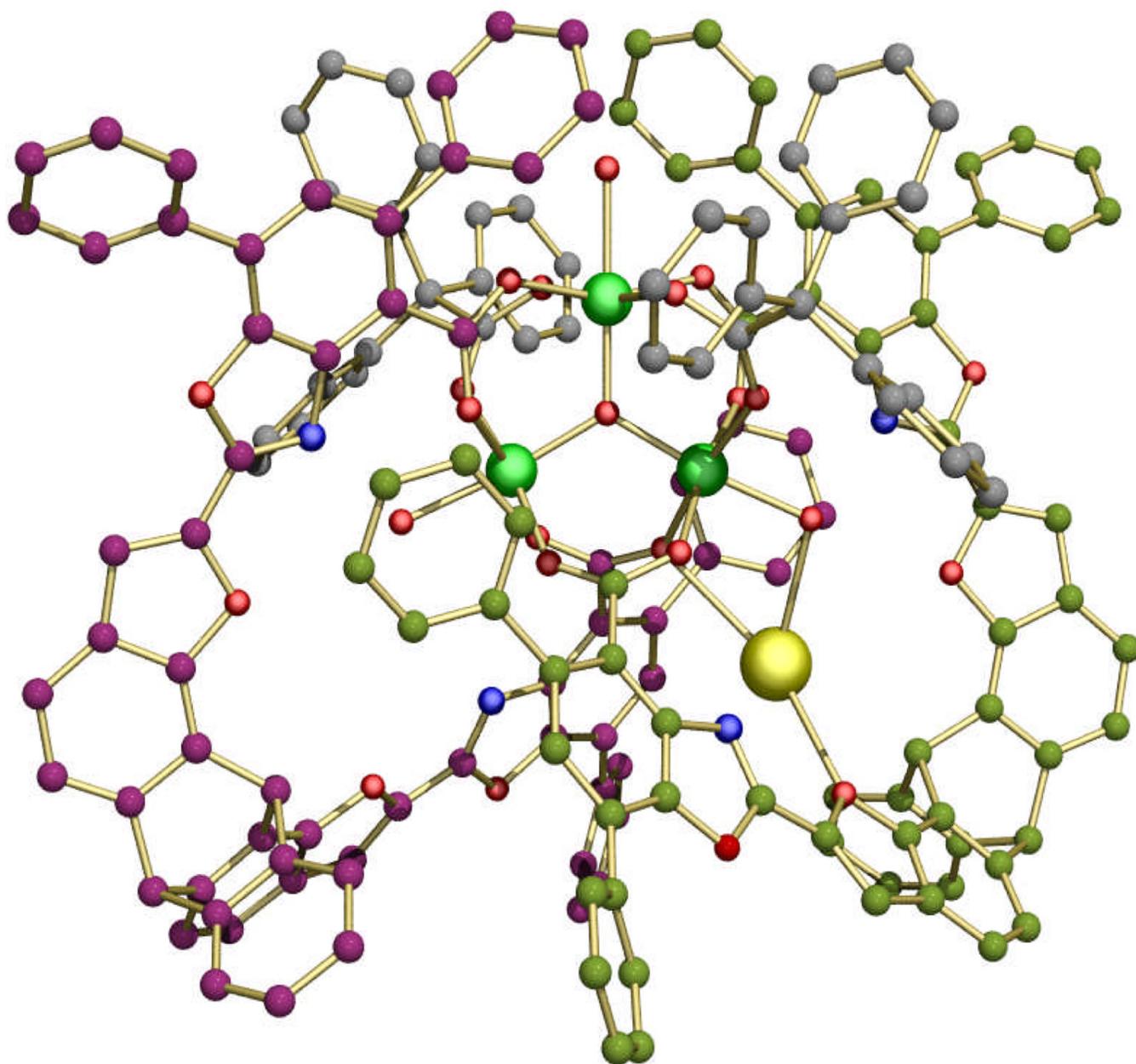
**Figure 1.**  
Basic iron acetate



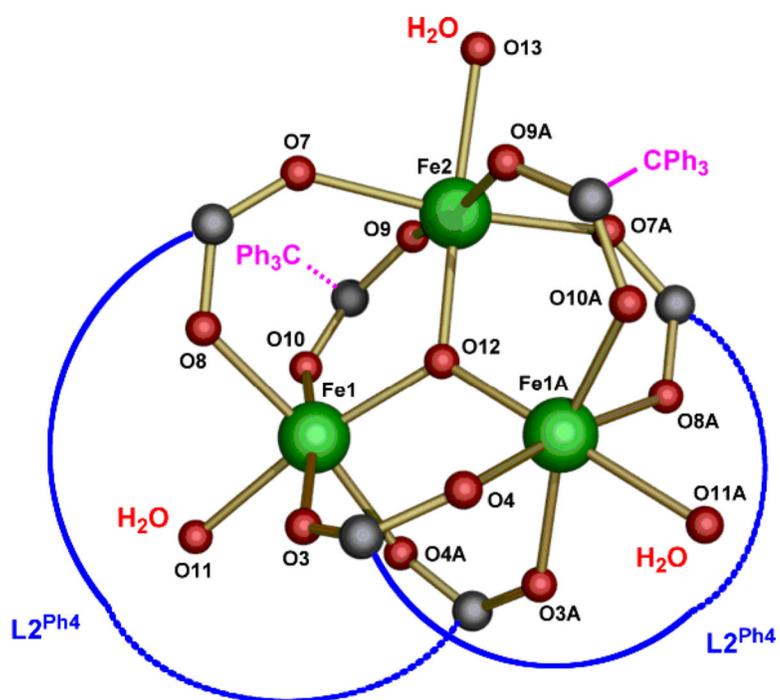
**Figure 2.**  
ligand **L1** and proposed diacid ligands



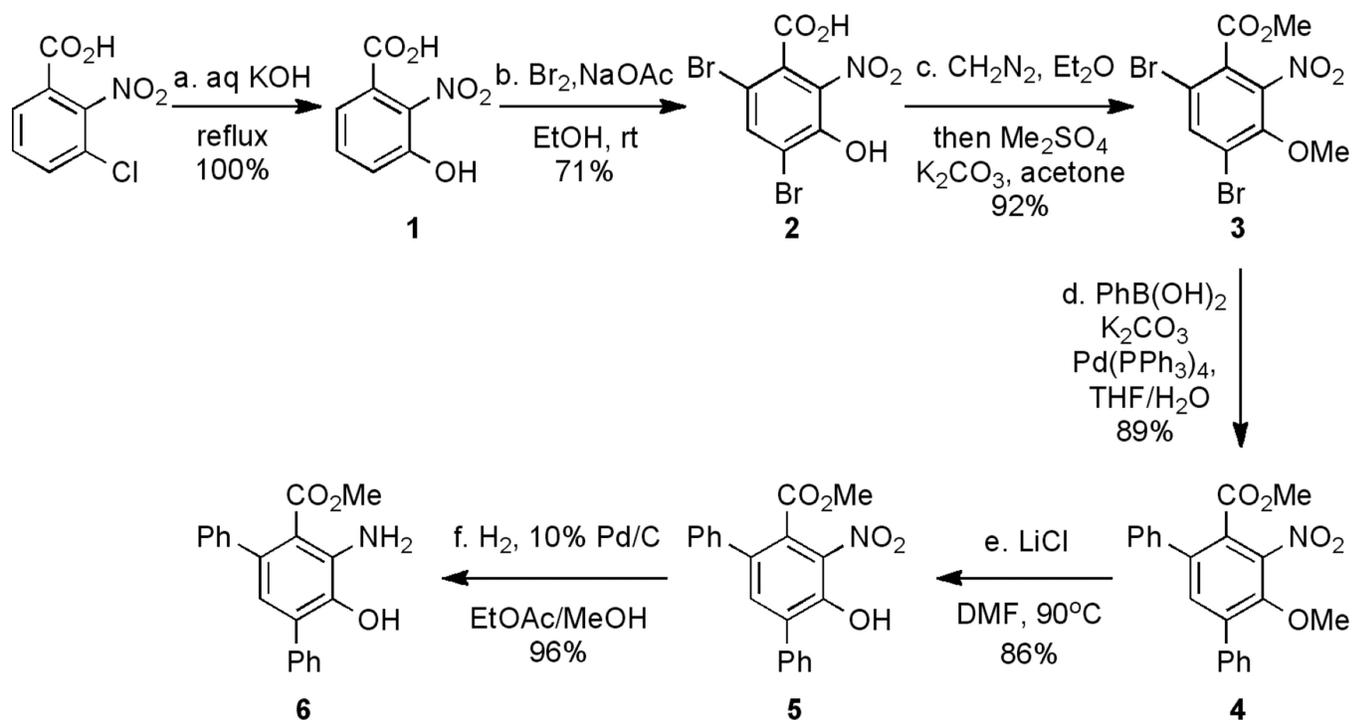
**Figure 3.** Thermal ellipsoid plot (50% probability) of X-ray structure of ligand **H<sub>2</sub>L<sub>2</sub>Ph<sub>4</sub>**. Hydrogens on carbon are omitted for clarity. Carbon, gray; oxygen, red; nitrogen, blue; hydrogen, wheat.



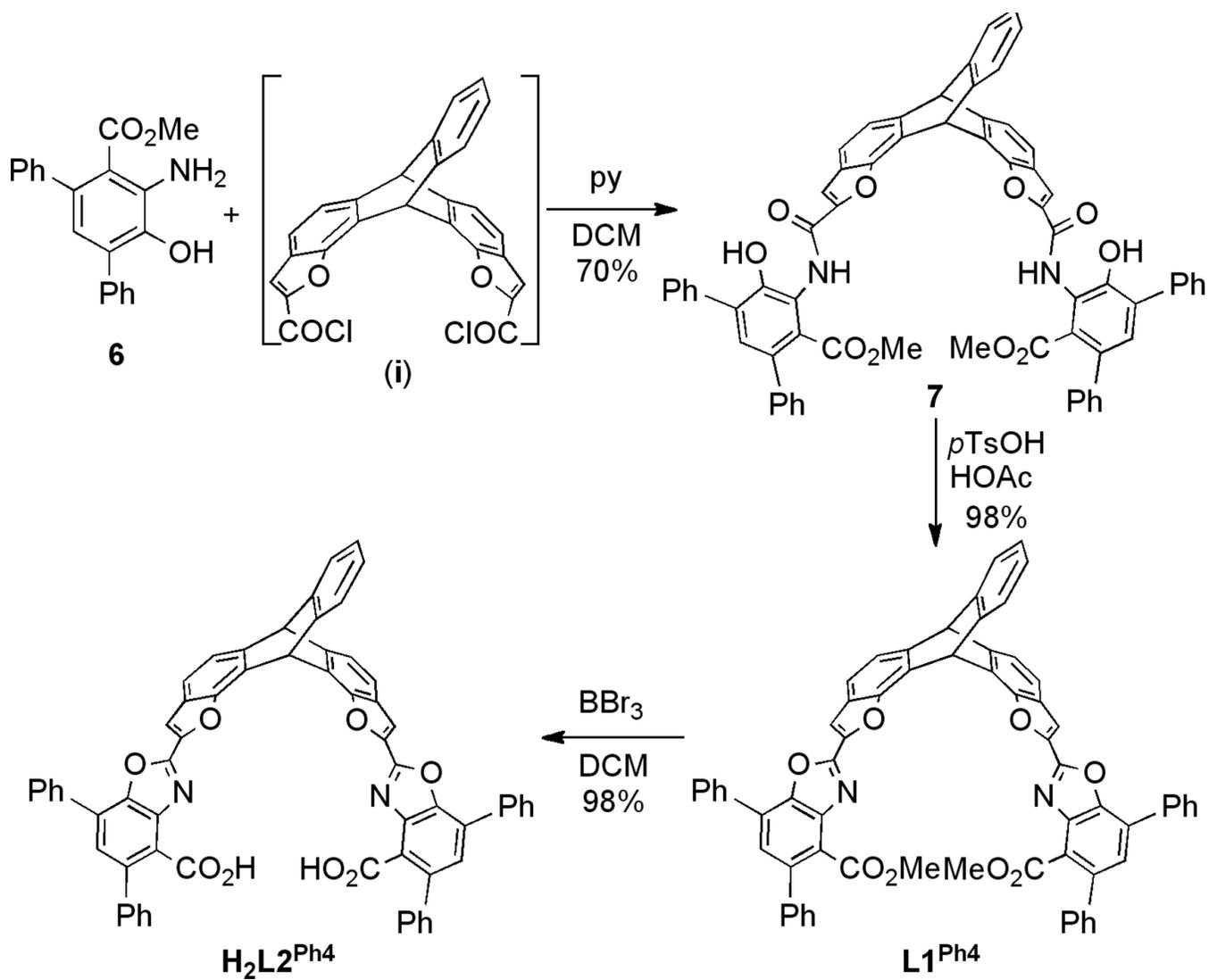
**Figure 4.** Ball-and-stick representation of the X-ray crystal structure of  $[\text{NaFe}_3(\text{L}2^{\text{Ph}4})_2(\mu_3\text{-O})(\mu\text{-O}_2\text{CPh})_2(\text{H}_2\text{O})_3](\text{OTf})_2$  (**8**). Hydrogen atoms, solvent molecules, and counter anions are omitted for clarity. The carbons of two  $(\text{L}2^{\text{Ph}4})^{2-}$  are colored pink and bright green. Iron, dark green; oxygen, red; nitrogen, blue; sodium, yellow. The depicted  $\text{Na}^+$  ion occurs at half-occupancy; the other ion, generated by a  $\text{C}_2$  axis, is not shown.



**Figure 5.**  
Core structure of complex 8.



**Scheme 1.**  
Synthesis of methyl anthranilate analog **6**.



Scheme 2.  
Synthesis of **H<sub>2</sub>L2<sup>Ph4</sup>**.

**Table 1**Mössbauer fits of two sites in complex **8**

	$\delta$ [mm/s]	$\Delta E_Q$ [mm/s]	$\Gamma$	Area [%]
<b>Site 1</b>	0.472±0.02	0.604±0.02	0.384	71
<b>Site 2</b>	0.684±0.02	0.600±0.02	0.252	29