Iron-Mediated Amination

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Multiple Aromatic Amination Mediated by a Diiron Complex

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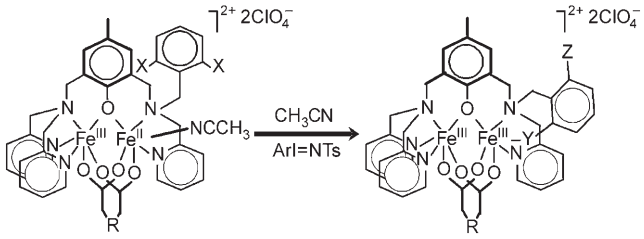
Metal-catalyzed amine transfer reactions constitute a field of active research to achieve carbon–nitrogen bond formation in synthetic organic chemistry. Following the original discovery by Sharpless and co-workers,[1] the biomimetic approach initiated by Breslow and Gellman[2] and Mansuy et al.[3] has attracted the interest of many groups. Nitrene addition to olefins and insertion into aliphatic C–H bonds have been reported in many instances;[4,5] however, very few examples of arene amination are known so far.[6–9] In particular, Que et al.[8] described the intramolecular aromatic amination of a phenyl-bearing ligand upon treatment of a ferrous complex with PhI=NTs (Ts = 4-methylphenylsulfonyl). It is worth noting that the yield of the amine transfer culminates at about 64% owing to hydrolysis of the iron nitrene active species, giving the hydroxylated product. Herein we present a diiron complex that can mediate the quantitative intramolecular amination of a benzyl group of the ligand without contamination of hydroxylated product, and that this amination produces both mono and bis(tosylamine) derivatives.

In the course of our biomimetic studies of iron centers in oxygenases, we developed mixed-valent $Fe^{II}Fe^{III}$ complexes of hexadentate binucleating ligands.[10] When the complex **1a** $[Fe_2(L)(mpdp)(H_2O)](ClO_4)_2$ (mpdp = 1,3-benzenedipropionate; for L see Scheme 1 with X = H) is reacted with oxygen donors such as *m*-chloroperbenzoic acid or iodosyl arenes it mediates an intramolecular oxygen atom transfer to the pendant benzyl residue of the ligand forming the *ortho*-hydroxybenzyl complex **2** (Scheme 1, with Y = O, Z = H).[11] In addition, we showed that complex **1b** $[Fe_2(L')(mpdp)(CH_3OH)](ClO_4)_2$ where the ligand bears a 2,6-dichlorobenzyl residue (Scheme 1, X = Cl) is able to catalyze the aziridination of various olefins and the sulfonamidation of thioanisole in good to excellent yields.[12] Herein we show that, when reacted with a tosyliminoaryliodinane[13] as nitrene source, **1a** is able to mediate the intramolecular aromatic amination of the unprotected benzyl residue to form the anilinate **3a**, which has been characterized by X-ray crystallography. Interestingly, the reaction furnished a second product **3b** in which two *ortho*-tosylamine groups have been incorporated. To our knowledge, the present complexes are the first binuclear complexes of an anilinato ligand.



Scheme 1. Reaction of mixed-valent diiron complexes (**1a**: X = H; **1b**: X = Cl) to give **2** (Y = O, Z = H) or **3** (**3a**; Y = NTs, Z = H; **3b**: Y = NTs, Z = NHTs). R = 1,3-$CH_2(C_6H_4)CH_2$.

Complex **1a** was prepared as previously described.[14,15] When an acetonitrile solution of **1a** was titrated with ArINTs, its blue color ($\lambda_{max} = 578$ nm, $\varepsilon = 1300\,M^{-1}cm^{-1}$) became progessively more intense, which corresponds to a two-fold increase in absorbance at about 585 nm and which was complete after the addition of 1.5(1) equivalents of ArINTs. Electrospray ionization mass spectrometry (ESI-MS) of the solution led to a spectrum that comprised two sets of three peaks (Figure 1). The first set is dominated by a peak at *m*/*z* 1028 which is due to the monocation $[Fe^{II}Fe^{III}(L\text{-}H{+}NTs)(mpdp)]^+$. In addition, two smaller peaks at *m*/*z* 514 and 1127 are associated to the dication $[Fe^{III}Fe^{III}(L\text{-}H{+}NTs)(mpdp)]^{2+}$ and the monocation $[Fe^{III}Fe^{III}(L\text{-}H{+}NTs)(mpdp)(ClO_4)]^+$, respectively. As is usual for these compounds, the mixed-valent form is produced within the mass spectrometer by reduction of the diferric complex. These observations paralleled the oxygenation of the benzyl group from iodosylarene[11] and suggests a tosylamine transfer onto the ligand.

A second set of three peaks is observed at *m*/*z* 598.5, 1197, and 1296 which corresponds to the analogous ions of a second compound $[Fe_2(L\text{-}2H{+}NTs{+}NHTs)(mpdp)]^{+/2+}$ that has two tosylamine groups incorporated. An NMR analysis of the reaction mixture after reduction by sodium iodide confirmed

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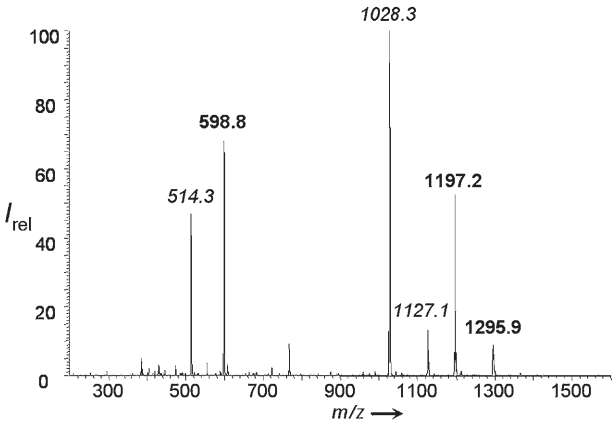

Figure 1. ESI-MS spectrum of the reaction mixture showing the peaks of complexes **3a** (italics) and **3b** (bold).

the presence of two diiron complexes (Figure 2a) in the ratio **3a**/**3b** 60:40.[16] The reaction solution was treated with sodium hydroxide to remove the iron atoms and the mixture of

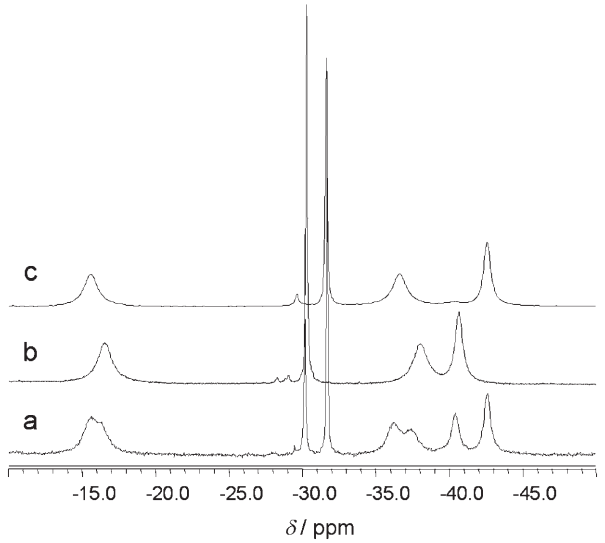

Figure 2. ^{1}H NMR spectra of the iodide-reduced reaction mixture (a) and complexes **3′a** (b) and **3′b** (c) in CD_3CN over the −10 to −50 ppm range.

ligands was submitted to a multiple-stage tandem ESI-MS analysis. The peaks of the two ligands were clearly identified at *m*/*z* 699 and 868, corresponding to the formula H(L-H+NHTs) and H(L-2H+2NHTs), respectively. They showed similar fragmentation patterns, which is in agreement with addition of the tosylamine groups to the benzyl group of the ligand. In particular, the bis(tosyl) ligand gave a fragment at *m*/*z* 429 corresponding to the bis(tosylamino)benzyl cation $[C_6H_3(NHTs)_2CH_2]^+$. The two ligands were then separated by reverse-phase HPLC and investigated by NMR spectroscopy. The *ortho*-benzylic proton appearing at $\delta = 7.19$ ppm in H(L-H+NHTs) was absent in H(L-2H+2NHTs) and the two *meta*-benzylic protons appearing at $\delta = 7.02$ and 7.53 ppm in H(L-H+NHTs) had merged to $\delta = 7.31$ ppm in H(L-2H+2NHTs), both features supporting a bis *ortho*-benzylic substitution in H(L-2H+2NHTs). Insertion of iron in the two ligands was performed as usual[14] and furnished the mixed valent derivatives $[Fe^{II}Fe^{III}(L\text{-}H+NTs)(mpdp)]^+$ (**3′a**) and $[Fe^{II}Fe^{III}(L\text{-}2H+NTs+NHTs)(mpdp)]^+$ (**3′b**).

The two complexes had almost identical UV-Vis spectra but slight differences could be detected by NMR spectroscopy. Indeed the *ortho*- and *para*-aniline resonances[17] (at ca. $\delta = -40.5$, −43 and −30, −32 ppm, respectively) were clearly distinguishable, as shown in Figure 2b,c. It is worth noting that the spectrum of **3′a** is identical to that obtained upon iodide reduction of **3a**. All in all, these experiments indicated that both tosylamine transfers occurred exclusively on the *ortho*-benzylic positions. Interestingly, neither NMR spectroscopy nor ESI-MS analyses revealed the formation of hydroxylated derivatives.

X-ray suitable crystals of the monosubstituted derivative **3a**-$(ClO_4)_2$ were grown from the reaction medium by slow evaporation. Figure 3 illustrates the structure (see also Supporting Information, Tables S1–S4) of the dication $[Fe_2(L\text{-}H+NTs)(mpdp)]^{2+}$. The most striking feature is the

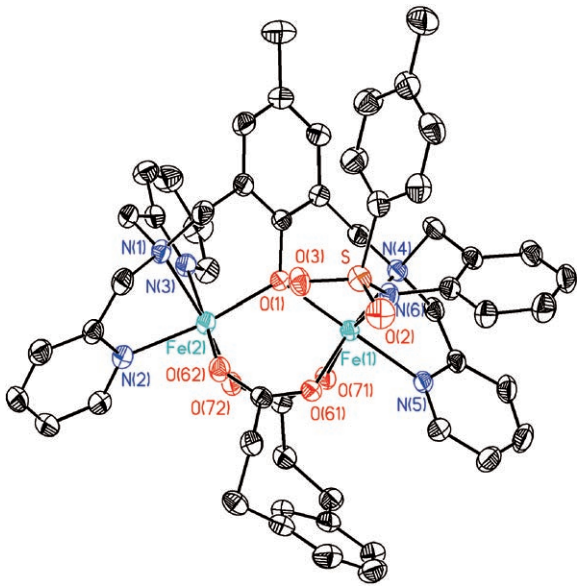

Figure 3. X-ray crystal structure of the dication **3a** $[Fe_2(L\text{-}H+NTs)(mpdp)]^{2+}$ (ellipsoids are set at 30% probability, and hydrogen atoms are omitted for clarity). Fe–ligand bond lengths [Å]: Fe(1)-O(61) 1.9639(17), Fe(1)-O(1) 2.0161(16), Fe(1)-N(6) 2.016(2), Fe(1)-O(71) 2.1230(18), Fe(1)-N(5) 2.130(2) Fe(1)-N(4) 2.182(2), Fe(2)-O(72) 1.9370(17), Fe(2)-O(62) 1.9909(19), Fe(2)-O(1) 2.0161(16), Fe(2)-N(3) 2.127(2), Fe(2)-N(2) 2.129(2), Fe(2)-N(1) 2.178(2), Fe(1)-Fe(2) 3.462.

insertion of the tosylamine group into the *ortho* position of the benzyl group and the coordination of the amine to the iron. Analysis of the bond lengths showed that the iron–ligand bonds average 2.072 Å and 2.063 Å for Fe1 and Fe2, respectively. These bonds are in the range expected for high spin ferric ions. In addition, it is noteworthy that the Fe2–N(Ts) bond is rather short (2.016 Å), which indicates that the benzyltosylamine is deprotonated and the compound is best described as a diferric anilinate. This valence description was

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confirmed by magnetic susceptibility and Mössbauer spectroscopy experiments (see Supporting Information, Figures S7, S8).

The electrochemical behavior of **3a** was investigated in acetonitrile by cyclic voltammetry and exhaustive electrolysis coupled with coulometry. Two reversible one-electron transfers were observed at -0.63 ($\Delta E_p = 80$ mV) and 0.10 V vs. Ag/Ag^+ 10^{-2} M ($\Delta E_p = 60$ mV) which can be assigned to the $Fe^{II}Fe^{II}/Fe^{II}Fe^{III}$ and $Fe^{II}Fe^{III}/Fe^{III}Fe^{III}$ couples, respectively (see Supporting Information, Figure S9). The low oxidation potential of **3a** is reminiscent of that of the corresponding *ortho*-phenolato derivative **2** (0.08 V)[17], showing that the tosylanilinato ligand is electronically very similar to its phenolato counterpart.

In summary, we have reported the very efficient and specific insertion of tosylamine groups into an aromatic residue mediated by a diiron complex. This is the first bimetallic system able to mediate such amine transfers. This reaction had been seldom achieved and often suffers from competition with the corresponding oxygen transfer. It is likely that it occurs through an iron(IV) imido derivative. Nevertheless, in the present case, this intermediate appears far less sensitive to hydrolysis as no trace of hydroxylation product has been detected even when the reaction was run in undried acetonitrile. This behavior may be due to the dinuclear nature of the active species which is probably analogous to that reported to mediate oxygen transfer reactions,[11] although the weak ability of **1a** to mediate oxygen atom transfers from iodosylarenes[11] is also likely to contribute. Interestingly a bis substitution occurs to a significant extent. This observation was unprecedented and opens the way to catalytic processes. The present results reveal significant differences in the reactivity of these binuclear complexes with the chemistry developed by the original porphyrin and mononuclear non-heme systems. The dinuclear nature of the present systems is most likely responsible for these differences and in depth mechanistic studies are underway to try and understand how these amine transfer reactions operate.

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[15] Experimental details and the structural description of **3a** are given in the Supporting Information. CDCC-656460 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[16] The yield of **3b** was reduced when only one equivalent of ArINTs was used, but it attained a maximum of 40% even with four equivalents. This behavior is due to the fact that **3a** and **3b** are formed by competitive mechanistic pathways. A complete mechanistic study of the reaction is currently in progress.
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