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Tying the alkoxides together: an iron complex of a new chelating bulky bis(alkoxide) demonstrates selectivity for coupling of non-bulky aryl nitrenes

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New chelating bis(alkoxide) ligand H₂[OO]^{Ph} and its iron(II) complex Fe[OO]^{Ph}(THF)₂ are described. The coordination of the ligand to the metal center is reminiscent of the coordination of two monodentate alkoxides in previously reported Fe(OR)₂(THF)₂ species. Fe[OO]^{Ph}(THF)₂ catalyzes selective and efficient dimerization of non-bulky aryl nitrenes to yield the corresponding azoarenes.

There is a growing interest in the transition metal-catalyzed synthesis of azoarenes. Azoarenes (ArN=NAr', "azo dyes") are highly colored compounds that have many existing industrial applications including as textile dyes/pigments, chemical indicators, and food additives; many additional potential applications are currently being pursued.² Established synthetic routes to azoarenes include azo coupling reaction,³ the Mills reaction, 4 the Wallach rearrangement, 5 and other routes. These preparative routes often require stoichiometric amounts of toxic and/or highly reactive co-reactants such as potassium dichromate, Caro's acid (H_2SO_5) , sodium amalgam, lead salts and others.^{1, 3-5} Efficient metal-catalyzed dimerization of nitrenes (derived from organoazides) constitutes a useful alternative to the above processes. 6-11 Selected transition metal catalysts for azoarene formation are presented in Figure 1. Most of the existing catalysts demonstrate limitations in the types of azoarenes they can produce. Uyeda's catalyst (B) exhibits the broadest scope of substrates, with the only limitation being bulky substrates (larger than mesityl). 11 Our group investigates group-transfer chemistry at [M(OR)₂] platforms, generally featuring two bulky monodentate alkoxide ligands. 12 We have reported that $Fe(OR)_2(THF)_2^{12a-c}$ (C, $OR = OC^tBu_2Ph$) served as an efficient catalyst for nitrene dimerization, although its reactivity was

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Figure 1. Examples of previously reported catalysts for azoarene formation

restricted to bulky aryl nitrenes featuring two ortho substituents. 10a Mechanistic studies suggested that alkoxide disproportionation (to yield tris(alkoxide) Fe(OR)₃ and bridging imido species $[Fe_2(OR)_2(\mu_2-NAr)]$) was at least in part responsible for this limitation. 10a To overcome this problem, we designed $Fe(OR')_2(THF)_2$ with a bulkier alkoxide OR' $(OR' = OC^{t}Bu_{2}(3,5-Ph_{2}Ph),$ **D**). 10b Consistent expectations, arresting the disproportionation route increased the overall scope of substrates to single ortho as well as metasubstituted aryl nitrenes, although the substrates lacking such substituents still exhibited poor reactivity (generally one turnover or less). 10b A different approach to the design of the more robust catalyst involves linking two monodentate alkoxides into a chelating ligand. Herein we present a preliminary report on the synthesis and reactivity of a new chelating bis(alkoxide) ligand H₂[OO]^{Ph} (1). We demonstrate that this ligand exhibits similar coordination chemistry to monodentate alkoxides, allowing us to conduct a comparative structure-activity study of different "Fe(OR)2" systems for nitrene coupling. Most importantly, Fe[OO]^{Ph}(THF)₂ exhibits complementary nitrene coupling reactivity to

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Figure 2. Top: Synthesis of 2. Bottom: structures of 1 and 2.

 $Fe(OR)_2(THF)_2/Fe(OR')_2(THF)_2$ (**C/D, Figure 1**), allowing efficient dimerization of non-bulky aryl nitrenes.

Bis(alkoxide) complexes featuring two bulky monodentate ligands generally exhibit a relatively broad angle between the alkoxides (RO-M-OR ~140 °, Figure 1), which leads to metal geometries intermediate between tetrahedral and seesaw. To model this disposition, we decided to employ the 1,4terphenyl structural motif, which was utilized by Agapie and coworkers in the synthesis of chelating ligands with a wide intra-ligand angle. 13 Chelating bis(alkoxide) ligand H₂[OO]^{Ph} (1) was synthesized in a three-step procedure (ESI) that involved initial synthesis of 1,4-bis(2-bromophenyl)benzene, 14 followed by lithiation with ^tBuLi, and finally reaction with benzophenone (72% yield, Scheme S1 in ESI). Phenyl substituents were chosen for the initial foray into the chelating bis(alkoxide) chemistry due to the anticipated crystallinity and slightly less steric hindrance compared with tert-butyl substituents. 1 was characterized by NMR spectroscopy, highresolution mass spectrometry, and X-ray crystallography (see ESI). X-ray crystallography confirms the overall connectivity and indicates anti geometry in the solid state with the alcohols on different sides of the central phenyl (Figure 2). ¹H NMR (C₆D₆) indicates a species of high symmetry in solution, consistent with either rapid interconversion of syn/anti forms, predominantly C_{2v} syn form, or predominantly C_{2h} anti form in solution. Supportive of the first hypothesis, a relaxed surface scan using DFT about the dihedral angle between the alkoxide arms suggests a low barrier of 9.5 kcal/mol with the syn isomer only 0.4 kcal/mol higher in energy than the anti isomer (see ESI Figure S46). A VT NMR study (conducted in CD_2Cl_2 in -60 – 20 °C range) demonstrates the presence of two isomers at low temperatures, as indicated by two well-resolved OH signals below -50 °C (Figure S25). Treatment of 1 with one equivalent precursor,¹⁵ Fe(N(SiMe₃)₂)₂(THF)_x followed recrystallization from CH2Cl2, leads to the isolation of light brown crystals of Fe[OO]^{Ph}(THF)₂ (2) in 82% yield. 2 was characterized by ¹H NMR spectroscopy, magnetic susceptibility measurements by Evans method, IR and UV-vis spectroscopy, X-ray crystallography, and elemental analysis (ESI).

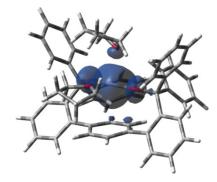


Figure 3. Spin density isosurface (iso = 0.002 au) plot for 2.

Solution magnetic susceptibility measurements suggest the compound has a high-spin Fe(II) center ($\mu_{\rm eff}$ = 4.8 μ B). Proton NMR contains 16 ligand signals (ESI), suggesting restricted rotation of the phenyl rings and an overall C_{2v} symmetry. The X-ray structure determination reveals a tetra-coordinate complex of Fe[OO]^{Ph}(THF)₂ composition. In contrast to the structure of 1, the ligand adopts a syn conformation in 2. The structure of 2 resembles the structures of the iron complexes with monodentate alkoxides, C and D, albeit with a significantly wider inter-alkoxide angle of 155.5(2) degrees (vs. $138.7(1)^{10a}$ and 141.5(1) for **C** and **D**, 10b respectively); the O(THF)-Fe-O(THF) angle is 88.8(2) degrees. These structural parameters suggest seesaw geometry at iron. No interaction between the metal and the central phenyl ring is observed (Fephenyl distance 3.1 Å). DFT optimization of 2 as a quintet agrees well with the experimental crystal structure and reinforces its assignment as a high-spin Fe^{II} species, as demonstrated by the spin density isosurface plot in Figure 3 with most of the spin density at the Fe ion or the alkoxide O atoms bonded to it. The higher energy singlet and triplet spin states have short Fe-C_{phenyl} distances of ~2.1 Å (see ESI **Figure S46, Table S3**), which suggests [OO] have allow metal-phenyl interactions in some species.

The reactivity of 2 in nitrene coupling was investigated and the results are presented in Figure 4. All reactions were carried out in C₆D₆ at 60 °C for 24 h using 10 mol% catalyst. The reactions were monitored by NMR spectroscopy, using hexamethylbenzene, trimethoxybenzene, hexafluorobenzene as an internal standard. The products were identified by ¹H NMR spectroscopy and confirmed by GC-MS; selected azoarenes were isolated and further characterized (ESI). Most notably, nitrene coupling reactivity exhibited by $Fe[OO]^{Ph}(THF)_2$ (2) is almost perfectly complementary to the reactivity exhibited by $Fe(OR)_2(THF)_2$ or $Fe(OR')_2(THF)_2$: while the previous catalysts were selective for the coupling of bulky aryl nitrenes, the present catalyst (2) demonstrates high to moderate yields for non-bulky substrates featuring para alkyl, trifluoro, or halo substituents; the conversion is quantitative for the phenyl azide (Figure 4). The formation of halosubstituted azoarenes is particularly noteworthy, as these groups can be later functionalized via cross-coupling. Although lower yields were observed for the p-nitro, p-acetyl, or pmethoxy groups, these are uncommon functional groups for metal-mediated formation of azoarenes.

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Figure 4. Nitrene coupling reactivity exhibited by 2.

In contrast, $Fe(OR)_2(THF)_2$ did not exhibit any reactivity with phenyl azide or *para*-substituted azides, and $Fe(OR')_2(THF)_2$ exhibited low reactivity at best. *Meta*-substituted 3,5-dimethylphenyl azide and 3-trifluoromethylphenyl azide exhibited relatively high yields (69% and 70% yields, respectively). In a sharp contrast, no reactivity with *ortho*-substituted (e.g. mesityl) azides was observed for $Fe[OO]^{Ph}(THF)_2$ (2), whereas both $Fe(OR)_2(THF)_2$ and $Fe(OR')_2(THF)_2$ demonstrated quantitative yield with mesityl azide.

What is the origin of the observed reactivity differences between $\text{Fe[OO]}^{\text{Ph}}$ and $\text{Fe(OR)}_2/\text{Fe(OR')}_2$ (**C/D**) systems? Due to the overall similarity of the three iron bis(alkoxide) systems, it is probable that the reaction of $\text{Fe[OO]}^{\text{Ph}}$ with aryl azides also proceeds via a metal-nitrene intermediate, whose formation and reactivity were computationally interrogated for the $\text{Fe(OR)}_2/\text{Fe(OR')}_2$ systems. Putative iron nitrenes with Ar = Ph and $\text{Ar} = 2,6\text{-Me}_2\text{Ph}$ (Mes surrogate) were optimized as quintets, based on our earlier modeling efforts, ¹⁰ for $[\text{OO]}^{\text{Ph}}$ and OR (**Figure 5**). In the less sterically bulky NPh species, the N of the nitrene is exposed for reactivity whereas it is blocked by one of the alkoxide phenyl groups for the ortho-substituted aryl substituent when the iron nitrene is supported by the $[\text{OO]}^{\text{Ph}}$ ligand (**Figure 5**, top). In contrast, the nitrene N remains

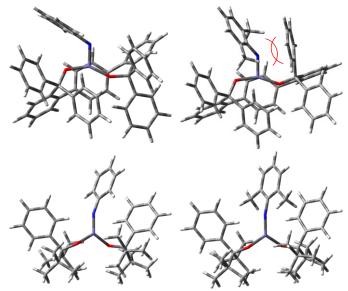


Figure 5. Optimized structures of putative iron nitrenes [Fe(L)(NAr)] supported by chelating [OO]^{Ph} ligand (top) or untethered OR ligands (bottom), using Ar=Ph (left) and Ar=2,6-Me₂Ph (right). All species were modeled as quintets.

accessible for both aryl substituents when FeNAr is supported instead by two OR groups (**Figure 5**, bottom). Therefore, we hypothesize that the inaccessibility of the nitrene when orthosubstitutents are present may be responsible for the lack of diazoarene formation in the presence of our new chelating ligand. Moreover, the Fe–N bond is mostly accessible by an incoming substrate from either face of the plane define by the alkoxides and nitrene in Fe(OR)₂(NAr), whereas the back face is blocked by the bridging terphenyl group and the front face is at least partially blocked by the alkoxide phenyl groups in Fe[OO]^{Ph}NAr. Even though these ligands give a similar trigonal planar coordination environments in both bis(alkoxide) environments, the spatial constraints imposed by the chelating ligand may provide an opportunity to control reactivity by limiting the approach of reactants to the nitrene moiety.

In conclusion, we have designed new chelating bis(alkoxide) ligand H₂[OO]^{Ph} with the 1,4-terphenyl bridge linking [OCPh₃]-like donors. Reaction of the ligand with an ironamide precursor led to the formation of a mononuclear complex Fe[OO]^{Ph}(THF)₂ closely related to the previously reported Fe(OR)2(THF)2 complexes with bulky monodentate alkoxides (OR = OC^tBu_2Ph and $OC^tBu_2(3,5-Ph_2Ph)$). Whereas the overall donors disposition at the iron(II) center is maintained, tying the alkoxides with the terphenyl bridge led to a pronounced difference in the steric nature at the metal site, which is illustrated by a nearly linear OAr-Fe-OAr angle (156°), as compared with ~140° in the more relaxed structures with monodentate ligands. Whereas the present "OCPh3" motif is not bulkier than the previously utilized OC^tBu₂Ar, it is likely the rigidity of the chelating system that prevents the rearrangement (i.e. rotation or geometry change) of the alkoxides. This difference in the nature of the active site is manifested in the reactivity of the resulting nitrene coupling catalysts. While Fe(OR)₂(THF)₂ complexes were able to couple bulky aryl nitrenes only (for OR = OC^tBu₂Ph) or mostly (for OR = OC^tBu₂(3,5-Ph₂Ph), Fe[OO]^{Ph}(THF)₂ is selective for coupling

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aryl nitrenes lacking *ortho* substituents; no reactivity with *ortho*-substituted (i.e. mesityl) azide took place. Successful formation of 13 different azobenzenes is presented. The difference in the reactivity is hypothesized to be due to the sterically congested active site of Fe[OO]^{Ph} , which interferes with the reactivity of putative "Fe[OO] Ph (= NMes)" species. Further mechanistic investigations of the present system, and studies on the reactivity of $\text{H}_2[\text{OO]}^{Ph}$ with other transition metals, are currently underway.

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Conflicts of interest

There are no conflicts to declare.

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