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COMMUNICATION

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 $H_2[OO]^{Ph}$ 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.¹ 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.¹ 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

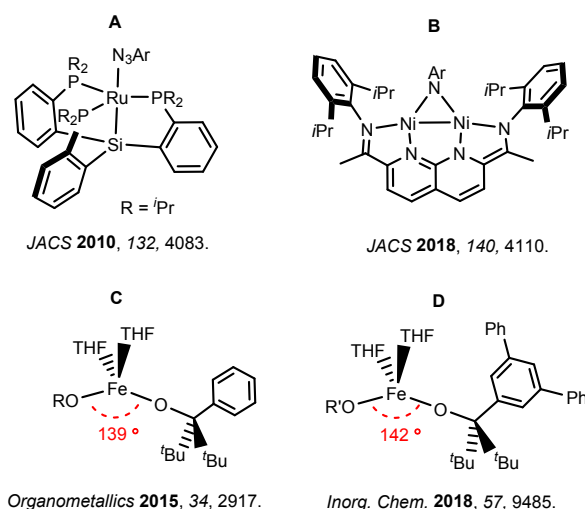


Figure 1. Examples of previously reported catalysts for azoarene formation

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' ($OR' = OC^tBu_2(3,5-Ph_2Ph)$, **D**).^{10b} Consistent with our expectations, arresting the disproportionation route increased the overall scope of substrates to single *ortho* as well as *meta*-substituted 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 $H_2[OO]^{Ph}$ (**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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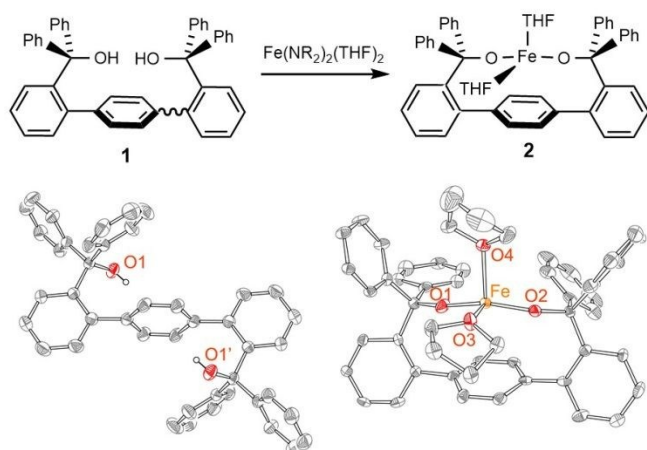


Figure 2. Top: Synthesis of **2**. Bottom: structures of **1** and **2**.

$\text{Fe}(\text{OR})_2(\text{THF})_2/\text{Fe}(\text{OR}')_2(\text{THF})_2$ (**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 ($\text{RO-M-OR} \sim 140^\circ$, **Figure 1**), which leads to metal geometries intermediate between tetrahedral and seesaw. To model this disposition, we decided to employ the 1,4-terphenyl 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 $\text{H}_2[\text{OO}]^{\text{Ph}}$ (**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 $t\text{BuLi}$, 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, high-resolution 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 (C_6D_6) 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 $-60 - 20^\circ\text{C}$ 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 of $\text{Fe}(\text{N}(\text{SiMe}_3)_2)_2(\text{THF})_x$ precursor,¹⁵ followed by recrystallization from CH_2Cl_2 , leads to the isolation of light brown crystals of $\text{Fe}[\text{OO}]^{\text{Ph}}(\text{THF})_2$ (**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).

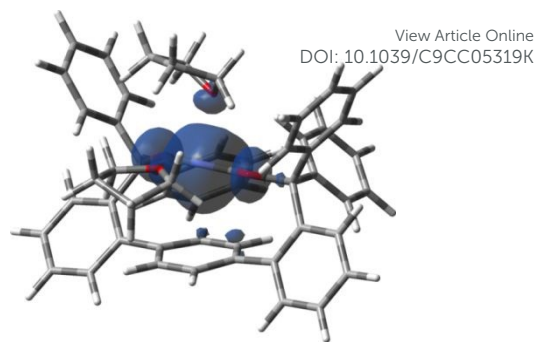


Figure 3. Spin density isosurface (iso = 0.002 au) plot for **2**.

Solution magnetic susceptibility measurements suggest the compound has a high-spin $\text{Fe}(\text{II})$ center ($\mu_{\text{eff}} = 4.8 \mu\text{B}$). 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 $\text{Fe}[\text{OO}]^{\text{Ph}}(\text{THF})_2$ 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 $\text{O}(\text{THF})\text{-Fe-O}(\text{THF})$ 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 (Fe-phenyl distance $3.1 \text{ \AA}$). 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 $\text{Fe-C}_{\text{phenyl}}$ distances of $\sim 2.1 \text{ \AA}$ (see ESI **Figure S46**, **Table S3**), which suggests $[\text{OO}]^{\text{Ph}}$ may 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 C_6D_6 at 60°C for 24 h using 10 mol% catalyst. The reactions were monitored by NMR spectroscopy, using trimethoxybenzene, hexamethylbenzene, or 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 $\text{Fe}[\text{OO}]^{\text{Ph}}(\text{THF})_2$ (**2**) is almost perfectly complementary to the reactivity exhibited by $\text{Fe}(\text{OR})_2(\text{THF})_2$ or $\text{Fe}(\text{OR}')_2(\text{THF})_2$: 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 halo-substituted 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 *p*-methoxy groups, these are uncommon functional groups for metal-mediated formation of azoarenes.

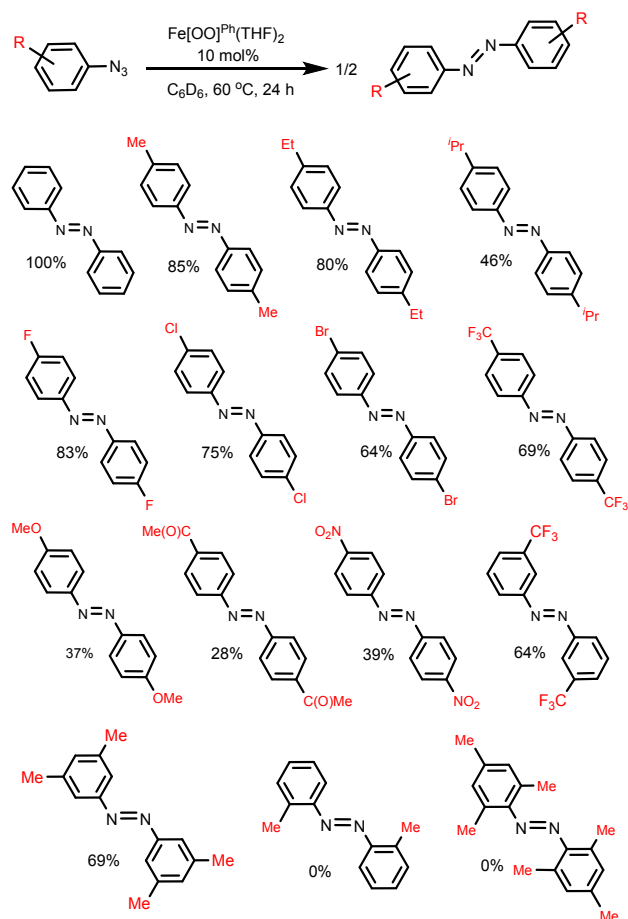


Figure 4. Nitrene coupling reactivity exhibited by 2.

In contrast, $\text{Fe}(\text{OR})_2(\text{THF})_2$ did not exhibit any reactivity with phenyl azide or *para*-substituted azides, and $\text{Fe}(\text{OR}')_2(\text{THF})_2$ 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 $\text{Fe}[\text{OO}]^{\text{Ph}}(\text{THF})_2$ (**2**), whereas both $\text{Fe}(\text{OR})_2(\text{THF})_2$ and $\text{Fe}(\text{OR}')_2(\text{THF})_2$ demonstrated quantitative yield with mesityl azide.

What is the origin of the observed reactivity differences between $\text{Fe}[\text{OO}]^{\text{Ph}}$ and $\text{Fe}(\text{OR})_2/\text{Fe}(\text{OR}')_2$ (**C/D**) systems? Due to the overall similarity of the three iron bis(alkoxide) systems, it is probable that the reaction of $\text{Fe}[\text{OO}]^{\text{Ph}}$ with aryl azides also proceeds via a metal-nitrene intermediate, whose formation and reactivity were computationally interrogated for the $\text{Fe}(\text{OR})_2/\text{Fe}(\text{OR}')_2$ systems. Putative iron nitrenes with $\text{Ar} = \text{Ph}$ 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

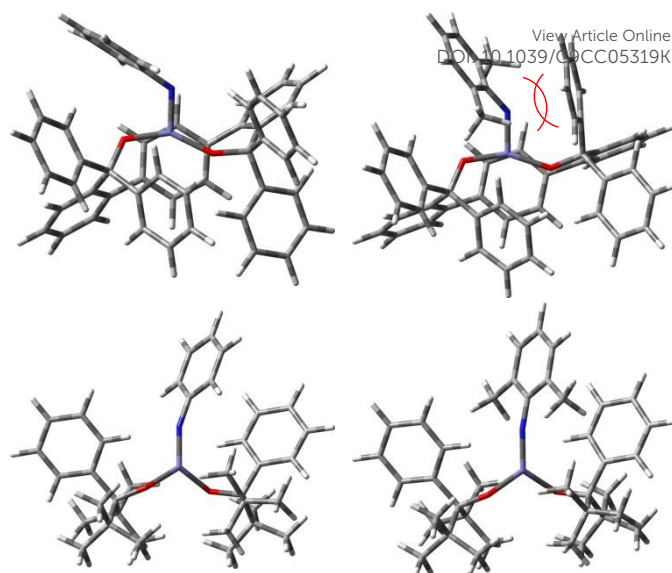


Figure 5. Optimized structures of putative iron nitrenes $[\text{Fe}(\text{L})(\text{NAR})]$ supported by chelating $[\text{OO}]^{\text{Ph}}$ ligand (top) or untethered OR ligands (bottom), using $\text{Ar} = \text{Ph}$ (left) and $\text{Ar} = 2,6\text{-Me}_2\text{Ph}$ (right). All species were modeled 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 *ortho*-substituents are present may be responsible for the lack of diazoarene formation in the presence of our new chelating ligand. Moreover, the $\text{Fe}-\text{N}$ bond is mostly accessible by an incoming substrate from either face of the plane define by the alkoxides and nitrene in $\text{Fe}(\text{OR})_2(\text{NAr})$, 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 $\text{Fe}[\text{OO}]^{\text{Ph}}\text{NAr}$. 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 $\text{H}_2[\text{OO}]^{\text{Ph}}$ with the 1,4-terphenyl bridge linking $[\text{OCPh}_3]$ -like donors. Reaction of the ligand with an iron-amide precursor led to the formation of a mononuclear complex $\text{Fe}[\text{OO}]^{\text{Ph}}(\text{THF})_2$ closely related to the previously reported $\text{Fe}(\text{OR})_2(\text{THF})_2$ complexes with bulky monodentate alkoxides ($\text{OR} = \text{OC}^t\text{Bu}_2\text{Ph}$ and $\text{OC}^t\text{Bu}_2(3,5\text{-Ph}_2\text{Ph})$). 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 $\text{OAr}-\text{Fe}-\text{OAr}$ angle (156°), as compared with $\sim 140^\circ$ in the more relaxed structures with monodentate ligands. Whereas the present “ OCPh_3 ” motif is not bulkier than the previously utilized $\text{OC}^t\text{Bu}_2\text{Ar}$, 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 $\text{Fe}(\text{OR})_2(\text{THF})_2$ complexes were able to couple bulky aryl nitrenes only (for $\text{OR} = \text{OC}^t\text{Bu}_2\text{Ph}$) or mostly (for $\text{OR} = \text{OC}^t\text{Bu}_2(3,5\text{-Ph}_2\text{Ph})$), $\text{Fe}[\text{OO}]^{\text{Ph}}(\text{THF})_2$ is selective for coupling

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 $\text{Fe}[\text{OO}]^{\text{Ph}}$, which interferes with the reactivity of putative " $\text{Fe}[\text{OO}]^{\text{Ph}}(=\text{NMe}_2)$ " species. Further mechanistic investigations of the present system, and studies on the reactivity of $\text{H}_2[\text{OO}]^{\text{Ph}}$ with other transition metals, are currently underway.

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Conflicts of interest

There are no conflicts to declare.

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An iron complex with a new chelating bis(alkoxide) ligand leads to an active nitrene dimerization catalyst for a variety of para- and meta-substituted azide precursors.

