

Project Title: **Catalyst design for small molecule activation of energy consequence**

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Potential impact relevant to DOE objectives: Our efforts towards rational catalyst design have focused on constructing catalytic sites at the molecular level. We have demonstrated that open shell configurations are necessary to effect small molecule activation within polynuclear cores supported by polyamide ligand frameworks. The high degree of tunability conferred both by our ligand design and our ability to make hetero-polynuclear reaction nodes gives us unprecedented control over a wide reaction space to fine tune reactivity. Ultimately, the frontier of this research program is to define the catalytic capabilities to transform small molecule substrates into viable chemical fuels using the described polynuclear clusters. We aim to improve our understanding of factors contributing to the promotion of productive small molecule activation/functionalization processes, further developing new classes of inorganic catalysts to synthesize value-added commodity chemicals via clean reaction routes.

Executive Summary

This project targets the conversion of ubiquitous small molecules (e.g. NO, CO, H₂O) into viable precursors to synthetic fuels. Current state of the art catalyst design has not directly targeted transition metal complexes capable of mediating the multi-electron redox processes necessary to reduce the overpotential (energy loss) required to achieve efficient activation of small molecule substrates. In this vein, a new strategy has been developed for the assembly of polynuclear architectures; allowing for the construction of tunable polymetallic centers that assemble easily within a pre-organized template (conferring stability, selectivity and tunability) that can effect multi-electron redox processes for reactions. Catalyst development has commenced with the following target design elements: (1) catalysts featuring multiple transition metal ions in the same reaction space to greatly expand accessible molecular redox capabilities; (2) catalysts are assembled in a polynucleating ligand framework that permits control over the cluster morphology as well as the local steric and electronic environment of the transition metal ions within the cluster. The high-tunability of the catalyst composition (metal content) and geometric flexibility has permitted a rigorous assessment of electronic-structure-to-function relationship to be developed, further guiding synthetic efforts to realize more potent catalysts. The numerous permutations possible showcase the high degree of generality to this approach with many synthetic handles to tune redox and reaction chemistry. Trinuclear complexes have been synthesized featuring homo- and hetero-trinuclear cores featuring a variety of first row transition metal ions (Cr→Ni). The molecular clusters have been shown to successfully mediate multi-electron redox processes in a cooperative fashion without requiring strong chemical reductants or oxidants. The reactive molecular complexes are being utilized to activate and breakdown the robust bonds within typical waste stream small molecules (e.g., greenhouse gases) and convert them into value-added commodity chemicals. Ultimately, the catalysts developed by this approach will be required to convert energy acquired via renewable resources (e.g., solar or wind) into synthetic fuels as an energy storage mechanism.

Final Report

Background. Small molecule substrates can be interconverted as a mechanism for advanced energy storage in conjunction with renewable energy sources. The type of chemistry and catalysis necessary to develop alternative energy sources rely on small molecule (e.g. H₂O, N₂, CO₂) activation processes. Activation of these substrates relies on mediation of multi-electron, multi-proton reaction sequences. Stepwise delivery of these reagents can incur large overpotential costs as high-energy intermediates are encountered, evidenced by the strong chemical oxidants and reductants commonly employed to initiate reactivity in molecular-based catalysts. One possible method to circumvent these high-energy pathways is to mediate *concerted* multi-electron reaction pathways, bypassing high-energy intermediates altogether.

General Strategy. This project seeks to develop a general approach for transforming ubiquitous small molecules (e.g., CO, CO₂) into viable building blocks for synthetic fuels through the development of a new class of polynuclear catalysts. Targeted catalyst design element include: (1) reaction site featuring multiple transition metals to expand accessible molecular redox capabilities; (2) polynucleating ligands are used to control cluster morphology as well as the local steric and electronic environment of the transition metal ions within the cluster. The high-tunability of the catalyst composition (metal content) and geometric flexibility has permitted a rigorous assessment of electronic-structure-to-function relationship to be developed, further guiding synthetic efforts to realize more potent catalysts. Specific aims for this project include: (1) design ligand platforms to proximally accommodate multiple metal centers; (2) establish the ability of the polynuclear complexes to mediate multi-electron redox transformations, both electrochemically and via small-molecule activation processes; and (3) develop the multi-electron, stoichiometric reactivity discovered into viable catalytic processes to transform small molecule substrates into value-added chemicals (e.g. fuels).

Design elements targeted in this proposal. As in Nature, our target reaction processes span both reduction and oxidation chemistry. The synthesis of methanol or liquid fuels from CO₂ (6e⁻/6H⁺), like water oxidation (4e⁻/4H⁺), requires the management and execution of multi-electron processes, thus requiring very specific catalytic capabilities (Table 1). Thus we are able to outline several desirable design elements for catalyst development: (1) *Organized self-assembly*. A modular ligand framework featuring multiple transition-metal binding sites may permit the construction of well-defined reaction sites, substituting in the capacity of a protein superstructure. (2) *Tunability*. One of the drawbacks of unchecked self-assembly in typical transition metal cluster synthesis is there are little means for controlling local metal coordination environments, limiting our ability to target specific classes of reactivity. General catalyst development strategy that permits both tunability and substrate selectivity in a predictable fashion to provide greater synthetic utility for both reductive and oxidative processes. (3) *Capacity for multi-electron activity*. A critical component to facilitating the key reactions of interest is to develop catalysts capable of efficiently mediating multi-electron redox processes. We hypothesize the polynuclear nature of the targeted complexes will expand the electronic reservoir available during reactions.

An ideal catalytic system would feature a tunable polymetallic center that assembles easily within a pre-organized template (conferring stability, selectivity and tunability) to effectively mediate multi-electron redox processes. Thus we sought to accomplish the following tasks during the grant lifetime: (1) Synthesize ligand platforms capable of binding multiple transition metal ions in the same proximal space. Examine the coordination chemistry of weak-field, dendritic ligand platforms to proximally accommodate multiple

metal centers, and determination of the resulting transition metal complex's electronic structure and capacity for multi-electron redox. (2) Establish the ability of the polymetallic clusters to bind small molecule substrates and mediate multi-electron redox transformations via small-molecule activation processes. (3) Develop the multi-electron, stoichiometric reactivity established into viable catalytic processes to transform small molecule substrates into value-added chemicals (e.g. fuels).

Summary of Results

Small molecule activation at polynuclear reaction sites

We have previously reported the synthesis and preliminary reactivity studies with a variety of small molecules.¹⁻³ We explored multielectron bond activation processes and oxidative group transfer to early transition metal clusters.⁴ While the divalent chromium cluster (^{tbs}L)Cr₃(thf) exhibits the same morphology as its all-ferrous analogue,^{2, 3} the [Cr₃] cluster does not exhibit the same strong, intracluster magnetic coupling exhibited by the iron variant.^{3, 5} The [Cr₃] cluster does exhibit nitrene extrusion from organic azides to afford terminal and bridging imido products depending on the azide organic moiety size (Figure 1). While mesitylazide breakdown affords the terminal imido in benzene, the sterically less demanding benzylazide affords the bridging imido. Remarkably, the reaction solvent can influence the reaction outcome. For example, mesitylazide cannot displace THF bound to the cluster when the reaction is run in THF, allowing only the azide γ -N to interact with the [Cr₃] face (determined by isotopic labeling of the N), leading to the three-electron N-atom excision to form the nitride (^{tbs}L)Cr₃(μ^3 -N) (Figure 1). As proposed, the early transition metal cluster featuring Cr^{II} centers can readily access 2 \rightarrow 4 electron oxidation processes. Bartholomew, A. K.; Juda, C. E.; Lin, B.; Betley, T. A. "Ligand-based control of single-site vs multi-site reactivity by a trichromium cluster." *Angew. Chem. Int. Ed.*, **2019**, 58, 5687-5691.

We established facile chalcogen excision using the all-ferrous cluster (^{tbs}L)Fe₃(thf).³ Formation of the parent oxo cluster was achieved by reduction of the cluster starting material by one electron via KC₈ addition, followed by treatment with pyridine N-oxide (Figure 2). Alternatively, addition of KOCPh₃ or KSCPh₃ resulted in oxide or sulfide excision with concomitant formation of Gomberg's dimer.⁶ The heavier chalcogenides were afforded by cluster reduction and subsequent treatment with elemental selenium or tellurium. From this study (currently under review),⁷ we were able to isolate the putative oxo cluster and fully characterize the complex in three oxidation levels [(^{tbs}L)Fe₃(μ^3 -O)]ⁿ (n : 0, -1, -2), providing the spectroscopic signatures for the oxo in a variety of oxidation states for identification in the O-atom excision to be pursued (*vide infra*). Our goal for this project is to generalize these processes and not rely on activated substrates to drive oxidative group transfer to the cluster reaction sites. This work is currently under review (Teesdale, J. J.; Greer, S. M.; Hill, S.; Betley, T. A. "Conferring magnetic anisotropy to high spin clusters." *Inorg. Chem.*)

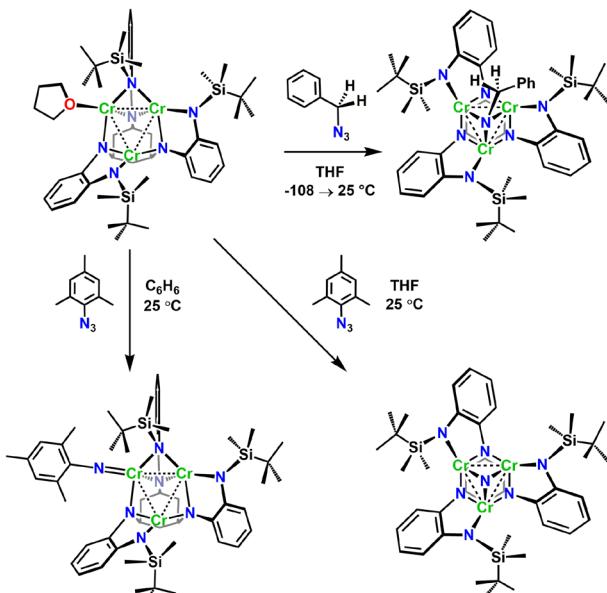


Figure 1. Azide reactivity of (^{tbs}L)Cr₃(thf) to yield bridging and terminal imidos as well as nitride excision from mesitylazide in THF.

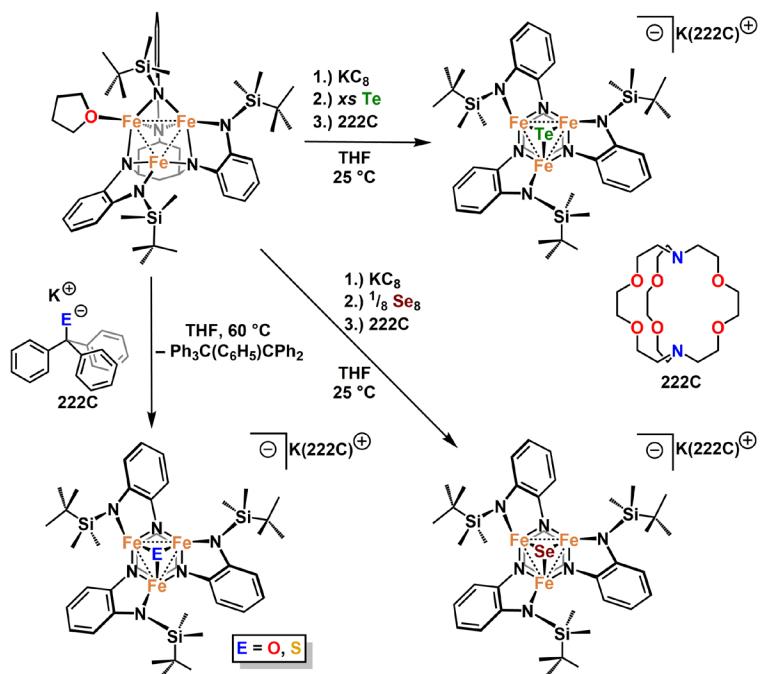


Figure 2. Oxo and chalcogenide transfer to $(^{tbs}L)Fe_3(\text{thf})$.⁷

paramagnetic resonance (EPR) with frequency-domain Fourier-transform EPR allowed an accurate quantification of the spin Hamiltonian parameters of the Fe_6 core. The combined high-resolution measurements on both powder samples and an oriented single crystal provide a quantitative measure of the isolated nature of the spin ground state in the Fe_6 molecule, as well as additional microscopic insights into factors that govern the quantum tunneling of its magnetization. Nehrkorn, J.; Greer, S. M.; Malbrecht, B. J.; Anderton, K. J.; Aliabadi, A. Krzystek, J.; Schnegg, A.; Holldack, K.; Herrmann, C.; Betley, T. A.; Stoll, S.; Hill, S. "Spectroscopic investigation of a metal-metal-bonded Fe_6 single molecule magnet with an isolated $S = 19/2$ giant-spin ground state." *Inorg. Chem.* **2021**, *60*, 4610-4622.

Bond activation and formation at binuclear complexes.

Polynuclear active sites are a common motif employed by enzymes to facilitate cooperative redox chemistry. For instance, diiron enzymes serve a variety of purposes in nature; examples include soluble methane monooxygenase (sMMO), an enzyme that promotes catalytic hydroxylation of organic substrates, and ribonucleotide reductase (RNR), which activates dioxygen in the reduction of ribonucleotides to the corresponding deoxyribonucleotides. Inspired by the cooperativity of these and similar enzymes, we developed a bimetallic scaffold to position metals proximally without the potential for metal–metal bond formation, thereby preserving the capacity for multi-electron reactions without substrate competition from intracluster M–M bonding. Specifically, we have utilized pacman structures, wherein the dinucleating architecture can support two metals proximally oriented to maximize their ability to perform cooperative chemistry. To this end, dicobalt (II) bridging mono-hydroxide and bis-hydroxide species have been synthesized and shown to impart interesting reactivity. Interconversion between these species was possible due to the lability of hydroxide bridges in the bis- μ -hydroxide, either by acid-base or redox reactions. Furthermore, when the bis-hydroxide species was oxidized twice with an oxidant like trityl chloride

Electronic structure of high-spin clusters

In a collaboration with Stefan Stoll and Stephen Hill, we examined the nature of M–M bonding within the high-spin clusters prepared in our lab. The metal–metal-bonded molecule $[Bu_4N][(^H L)_2Fe_6(\text{dmf})_2]$ (Fe_6) was previously shown to possess a thermally isolated spin $S = 19/2$ ground state and found to exhibit slow magnetization relaxation below a blocking temperature of 5 K. Examining this molecule using a comprehensive spectroscopic investigation of this unique single-molecule magnet (SMM), combining ultrawideband field-swept high-field electron

(Ph_3CCl), full convergence to the corresponding dicobalt(II) dichloride species along with expulsion of the hydroxide bridges to form Ph_3COH was observed (Figure 3). We anticipated that the edge-sharing, square-planar Co^{II} sites would distort into octahedral geometries with the formation of $\text{Co}-\text{Co}$ bond. Rather, the radical character enhancement at the bridging hydroxide ligands results in their release to regenerate cobalt(II) rather than stabilizing higher valent cobalt centers, unveiling the potential for oxygen-group atom transfer reactivity. We are examining the propensity for hydroxyl radical release and how that can be utilized to drive oxidative chemistry. A manuscript discussing this work is under review (Johnson, E. J., Betley, T. A. "Redox-triggered hydroxy release from a dicobalt bis-hydroxo complex." *Chem. Sci.*).

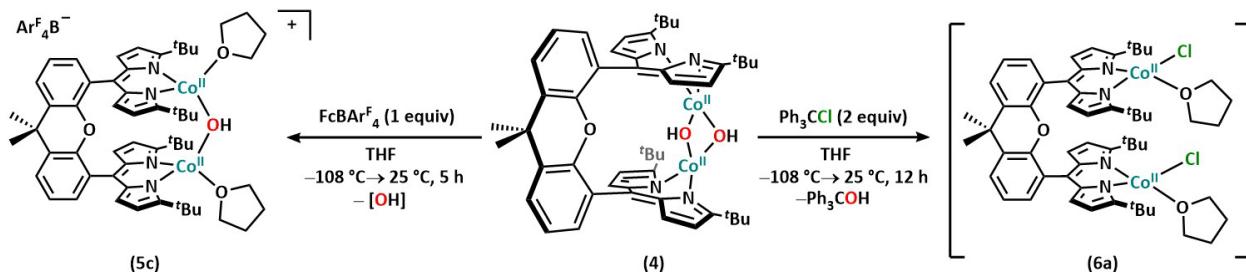


Figure 3. Dicobalt oxidation chemistry.

Redox load distribution in cluster reactivity

Identifying the redox states within polynuclear cofactors in biology is critical for elucidating substrate binding sites. Multiple-wavelength, anomalous X-ray diffraction (MAD) has been used to address the redox states within the polynuclear cofactors in nitrogenase. While MAD provides a site-specific analytical technique to resolve differences in relative redox states within molecular species, we note that rigorous application of this technique on well-defined synthetic iso- and mixed-valent clusters has not been performed. Our report illustrates the large variation observed for nominally isovalent sites, thus providing a much-needed calibration on what to expect for resolving redox load distribution within cluster materials.

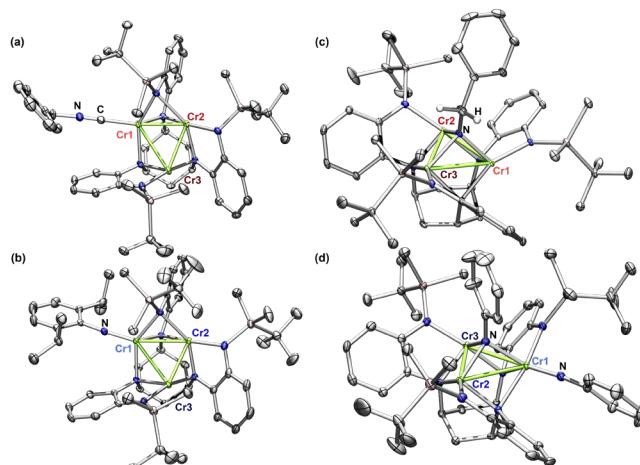


Figure 4. Solid-state molecular structures (a) $(^{\text{tbs}}\text{L})\text{Cr}_3(\mu^1\text{-CNBn})$ (4); (b) $(^{\text{tbs}}\text{L})\text{Cr}_3(\mu^1\text{-NDipp})$ (2); (c) $(^{\text{tbs}}\text{L})\text{Cr}_3(\mu^3\text{-NBn})$ (3); and (d) $(^{\text{tbs}}\text{L})\text{Cr}_3(\mu^3\text{-NPh})(\mu^1\text{-NPh})$ (5). Structures are presented with ellipsoids at 50% (C gray, N blue, H white, Cr green) at 100 K with 50% probability ellipsoids.

The unusual chemistry of a sterically hindered trichromium complex allowed for the isolation of two structurally isomeric trichromium imides: the highly asymmetric terminal imide $(^{\text{tbs}}\text{L})\text{Cr}_3(\mu^1\text{-NDipp})$ and the more symmetric bridging imide $(^{\text{tbs}}\text{L})\text{Cr}_3(\mu^3\text{-NBn})$ (Figure 4). Given that both molecules are formally mixed-valent and share the same molecular oxidation state, this pair of complexes presented a prime opportunity to probe the relationship between structural and redox isomerism. Along with the homovalent reference $(^{\text{tbs}}\text{L})\text{Cr}_3(\mu^1\text{-CNBn})$ and further-oxidized bisimide $(^{\text{tbs}}\text{L})\text{Cr}_3(\mu^3\text{-NPh})(\mu^1\text{-NPh})$

(Figure 4), both imide isomers were examined by multiple-wavelength anomalous diffraction (MAD) to determine the redox load distribution by the free refinement of atomic wavelength scattering factors (Figure 5). Despite their compositional similarities, the terminal and bridging imido complexes were found to have distinct oxidation distributions, with the bridging imide showing uniform oxidation of all three Cr sites while the terminal imide shows oxidation at only two Cr sites. Further oxidation from the bridging imide to the bisimide is only born at the Cr site bound to the second, terminal imido fragment. Thus, depending on the structural motifs present in each Cr_3 complex, MAD revealed complete localization of oxidation, partial localization, and complete delocalization, all supported by the same hexadentate ligand scaffold.

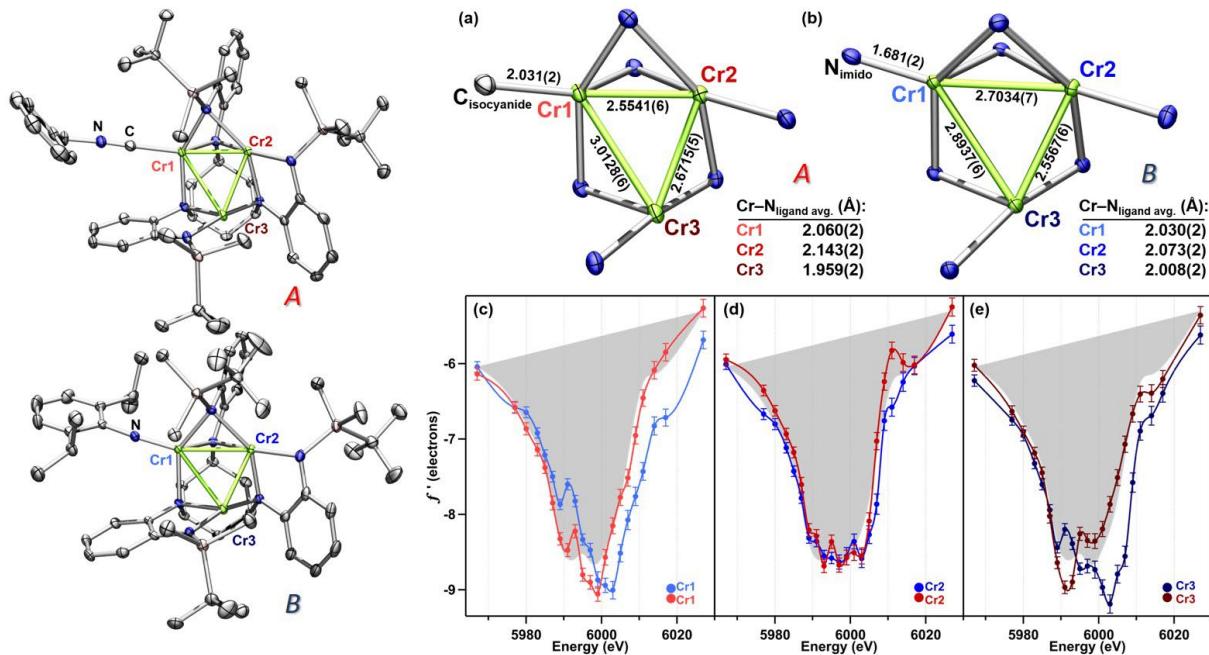


Figure 5. Crystal structure of and core bond metrics of (a) $(^{\text{tbs}}\text{L})\text{Cr}_3(\text{CNBn})$ (**A**) and (b) $(^{\text{tbs}}\text{L})\text{Cr}_3(\text{NDipp})$ (**B**). Anomalous scattering factor f' for each chromium center (Cr1, Cr2, Cr3) determined from refinement of the diffraction data collected at 100 K and using a full structure solution collected at 30.5 keV as a reference for $(^{\text{tbs}}\text{L})\text{Cr}_3(\text{CNBn})$ and $(^{\text{tbs}}\text{L})\text{Cr}_3(\text{NDipp})$. (c–e): Direct comparison of the anomalous scattering factor f' for (f) Cr1, (g) Cr2, and (h), Cr3 sites of $(^{\text{tbs}}\text{L})\text{Cr}_3(\text{CNBn})$ (**red**) and $(^{\text{tbs}}\text{L})\text{Cr}_3(\text{NDipp})$ (**blue**).⁵⁴

We applied the resonant diffraction technique to assess the redox distribution of the seemingly redox-isolated trichromium clusters discussed in Section 3.1.1. An all- Cr^{II} cluster $(^{\text{tbs}}\text{L})\text{Cr}_3(\text{CNBn})$ was selected to compare with the isostructural, doubly oxidized terminal imido cluster $(^{\text{tbs}}\text{L})\text{Cr}_3(\text{NDipp})$ (Figure 6). The anomalous scattering factors (f') for each of the Cr atoms in the two clusters are overlaid in panels c–e in Figure 8, where the gray area is from a reference complex of Cr^{II} to provide a visual reference. As expected, the imido-bearing Cr1 exhibits a shift to higher energy (reflecting higher local oxidation state) than the isocyanide-bearing Cr1 (Figure 8c). While the two Cr2 center scattering factor envelopes are nearly coincident, we observe an unanticipated shift to higher energy for the Cr3 site in imido-bearing cluster. Thus, we conclude that the two-electron oxidation arising from nitrene (NDipp) capture is delocalized between the Cr1 and Cr3 sites, while Cr2 is largely unchanged. The resonant diffraction data reveal that the clusters can distribute redox load across the cluster face, even when close M–M interactions are absent as in the present case. See publications: Bartholomew, A. K.; Teesdale, J. J.; Hernández Sánchez, R.; Malbrecht, B.; Juda, C. E.; Ménard, G.; Bu, W.; Iovan, D. A.; Mikhailine, A. A.; Zheng, S.-L.; Sarangi, R.;

Wang, S. G.; Chen, Y.-S.; Betley, T. A. "Exposing the inadequacy of redox formalisms by resolving redox inequivalence within isovalent clusters." *Proc. Nat. Acad. Sci.*, **2019**, *116*, 15836-15841; and Bartholomew, A. K.; Musgrave, R. A.; Anderton, K. J.; Juda, C. E.; Dong, Y.; Bu, W.; Wang, S.-Y.; Chen, Y.-S.; Betley, T. A. "Revealing redox isomerism in trichromium imides by anomalous diffraction." *Chem. Sci.* **2021**, *21*, 15739-15749.

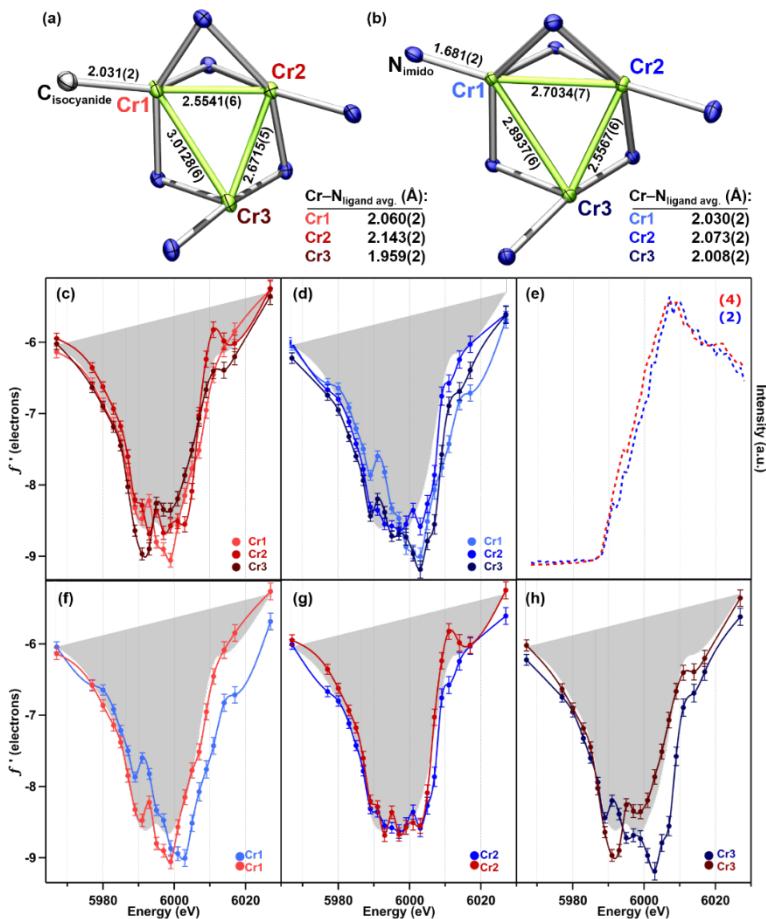


Figure 6. Crystal structure cores with bond metrics of (a) $(^{tbs}L)Cr_3(CNBn)$ and (b) $(^{tbs}L)Cr_3(NDipp)$. Anomalous scattering factor f' for each chromium center determined from refinement of the diffraction data collected at 100 K and using a full structure solution collected at 30.5 keV as a reference for (c) $(^{tbs}L)Cr_3(CNBn)$ and (d) $(^{tbs}L)Cr_3(NDipp)$. (e) Single-crystal X-ray fluorescence scans of **4** and **2** collected around the Cr K-edge in steps of 1 eV at 100 K. (f-h): Direct comparison of the anomalous scattering factor f' for (f) Cr1, (g) Cr2, and (h), Cr3 sites of **4** and **2**.

Conclusions

The results presented within this funding period allowed us to examine the utility of small molecule activation processes using cluster-based reaction sites. Bimetallic, trinuclear, and hexanuclear clusters were examined for their cooperative redox properties, their reactivity with small molecules, and the resulting electronic structures unique to these M–M bonded entities. Overall, the work points to new strategies for cooperative small molecule activation, taking lessons from both heterogeneous catalysts and the metallocofactors found in nature.

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