

ligand undergoes reductive coupling with the incoming substrates to form ring-closed manganabicyclodecane complexes with high-spin  $S = 5/2$  spin states. This ligand-based reactivity is consistent with the high degree of spin localization within the dtvms  $\pi^*$  orbitals, which is in line with the authors' calculations and the suggestion that substantial electron density is present on the olefin ligands. Similarly, ligand-based reactions involving the dtvms double bonds are observed in the presence of  $H_2$ . Under an atmosphere of  $H_2$ , one hydrogen atom is added to each of the terminal carbon atoms of the dtvms arms, whereas the internal carbon atom of each arm remains coordinated to Mn as an alkyl ligand. This latter reaction is a particularly exciting development, especially if dissymmetric hydrogenation, where one  $H_2$  molecule is cleaved over two distinct olefins, can be developed in a general fashion.

With a constant push for new transition-metal complexes to catalyze difficult transformations, Deng and co-workers

present a unique class of low-coordinate Mn complexes capable of performing intriguing partial hydrogenations as well as unusual ring-formation reactions. As with many important discoveries, this reactivity was enabled by the quest to answer a simple question—what are the nature and properties of Mn centers in low-coordinate, low-valent environments? With this article by Deng and co-workers in *Chem*, some answers to this question are revealed and potentially open new avenues for the efficient synthesis of other complex molecules.

1. Hebrard, F., and Kalck, P. (2009). Cobalt-catalyzed hydroformylation of alkenes: generation and recycling of the carbonyl species, and catalytic cycle. *Chem. Rev.* *109*, 4272–4282.
2. Burdett, J.K. (1975). New method for the determination of the geometries of binary transition metal complexes. *Inorg. Chem.* *14*, 375–382.
3. Elian, M., and Hoffmann, R. (1975). Bonding capabilities of transition metal carbonyl fragments. *Inorg. Chem.* *14*, 1058–1076.
4. Poliakoff, M., and Turner, J.J. (1974). Structure and reactions of matrix-isolated tetracarbonyliron(0). *J. Chem. Soc., Dalton Trans.* *0*, 2276–2285.
5. See for example: Ung, G., Rittle, J., Soleilhavoup, M., Bertrand, G., and Peters, J.C. (2014). Two-coordinate  $Fe^0$  and  $Co^0$  complexes supported by cyclic (alkyl)(amino)carbenes. *Angew. Chem. Int. Ed.* *53*, 8427–8431.
6. Kidd, D.R., Cheng, C.P., and Brown, T.L. (1978). Formation and properties of substituted manganese carbonyl radicals. *J. Am. Chem. Soc.* *100*, 4103–4107.
7. Church, S.P., Poliakoff, M., Timney, J.A., and Turner, J.J. (1981). Synthesis and characterization of the pentacarbonylmanganese(0) radical,  $Mn(CO)_5$ , in low-temperature matrices. *J. Am. Chem. Soc.* *103*, 7515–7520.
8. Agnew, D.W., Moore, C.E., Rheingold, A.L., and Figueroa, J.S. (2015). Kinetic destabilization of metal-metal single bonds: isolation of a pentacoordinate manganese(0) monoradical. *Angew. Chem. Int. Ed.* *54*, 12673–12677.
9. Cheng, J., Chen, Q., Leng, X., Ouyang, Z., Wang, Z., Ye, S., and Deng, L. (2018). The stabilization of three-coordinate formal Mn(0) complex with NHC and alkene ligation. *Chem* *4*, this issue, 2844–2860.
10. Soleilhavoup, M., and Bertrand, G. (2015). Cyclic (alkyl)(amino)carbenes (CAACs): stable carbenes on the rise. *Acc. Chem. Res.* *48*, 256–266.

## Preview

# Metalloenzyme Mimicry at the Nodes of Metal-Organic Frameworks

Qi Sun,<sup>1</sup> Briana Aguila,<sup>1</sup> and Shengqian Ma<sup>1,\*</sup>

**In this issue of *Chem*, Dincă and co-workers show that the node of the metal-organic framework MFU-4l can be modified by anion exchange to serve as a biomimetic model of carbonic anhydrase given the similarity in their ligand fields. The resulting material, which has reactivity characteristics of the enzyme, gives great promise for CO<sub>2</sub>-related applications.**

Enzymes, nature's creation of catalysts, show extreme activity and selectivity for a range of chemical conversions. However, even when an enzyme is identified

as being useful for a given reaction, its extensive application is often hampered by its lack of long-term operational stability and also by difficulties

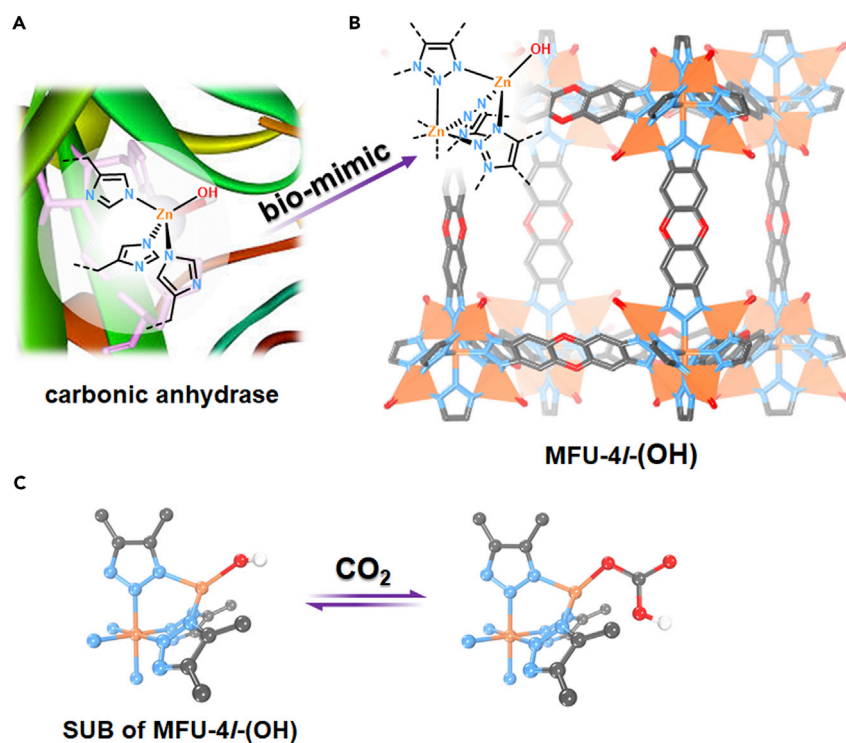
in recovery and recycling.<sup>1</sup> Advances have been made in biotechnology to allow for enzyme production at commercially acceptable prices and manipulation of them such that they exhibit the desired properties with regard to substrate specificity, activity, selectivity, and stability. Nevertheless, only a handful of successful paradigms that function properly have been synthesized. To overcome this ambiguity, biomimicry provides rational solutions through the incorporation of active-site synthetic analogs of enzymes in

<sup>1</sup>Department of Chemistry, University of South Florida, 4202 East Fowler Avenue, Tampa, FL 33620, USA

\*Correspondence: [sqma@usf.edu](mailto:sqma@usf.edu)

<https://doi.org/10.1016/j.chempr.2018.11.017>





**Figure 1. Structure Comparison between Carbonic Anhydrase and the SBU in MFU-4l(OH), as well as the Peripheral Zinc Structure in MFU-4l(OH) before and after CO<sub>2</sub> Adsorption**

(A and B) Structure of (A) the active site in CA and (B) MFU-4l(OH).

(C) Proposed scheme of reversible CO<sub>2</sub> hydrolysis reaction catalyzed by MFU-4l(OH) (orange, Zn; blue, N; gray, C; red, O; hydrogen is omitted for clarity).

suitable matrices by taking advantage of the versatility of synthetic chemistry.<sup>2</sup> Metal-organic frameworks (MOFs) are envisioned as the most promising candidate for this purpose.<sup>3–5</sup> MOFs are highly tunable nanoporous network compounds composed of inorganic nodes connected by organic linkers, and they offer tremendous potential for rational material design.<sup>6</sup> Their crystalline structures trace out topological backbones onto which desired functionalities can be introduced, either as functional moieties on the organic linkers or through the choice of metal nodes. The molecular-level structural control and modularity possible with MOFs allow for a hydrophobic or hydrophilic confined environment akin to natural enzymes, as well as offer an ordered distribution of highly dense substrate-accessible active catalytic sites throughout the architecture. In

addition, the higher stability of MOFs than of enzymes potentially leads to the broader use of biomimetic chemistry in industrially relevant applications.

Carbonic anhydrase (CA) is a ubiquitous zinc metalloenzyme that catalyzes the reversible hydration of CO<sub>2</sub> with an exceptional turnover rate of 10<sup>6</sup> per second, one of the fastest rates in enzyme catalysis.<sup>7</sup> To expand their utilization, researchers have therefore employed a large variety of tridentate ligands in efforts to obtain synthetic analogs of CA. Among them, the hydroxide complex Tp<sup>tBu,Me</sup>ZnOH (Tp = tris(pyrazolyl)hydroborate) has also been shown to be a functional analog of CA. Unfortunately, these systems lack heterogeneous analogs with similar activities, significantly hindering their industrial use. Given the similar ligand fields, the nodes

of MOFs are attractive sites for mimicking metalloenzymes. In this issue of *Chem*, Dincă and co-workers took the lessons learned from these homogeneous systems and targeted the material MFU-4l (Zn<sub>5</sub>Cl<sub>4</sub>(BTDD)<sub>3</sub>, where H<sub>2</sub>BTDD = bis(1H-1,2,3-triazolo[4,5-b],[4',5'-i])dibenzo[1,4]dioxin).<sup>8</sup> The secondary building unit (SBU) of this triazole-based MOF features facial coordination of Zn<sup>2+</sup> by three nitrogen atoms and is a scorpionate unit shown to structurally and functionally emulate the Tp-like environments within this MOF (Figures 1A and 1B).

In this paper, the benefits of using MOFs as a biomimetic platform are at the forefront: pore environments and structural tunability, site isolation, high surface area, and periodicity are all highly sought-after attributes for any efficient heterogeneous catalyst. The crystalline nature of MOFs offers opportunities to use their nodes as structurally characterizable active sites where mechanistic details of a catalytic process can be teased out, allowing for rational design and thereby improved overall efficiency. Herein, the structure of MFU-4l lends itself perfectly as the platform for mimicking CA for two primary reasons: (1) the SBUs in this material feature four peripheral zinc chloride sites that are coordinated by three triazoles in C<sub>3</sub> symmetry analogous to the Tp ligand and, accordingly, CA, and (2) the metal node of MFU-4l can be further modified by anion exchange to serve as a biomimetic model of CA. The original terminal N<sub>3</sub>Zn–Cl centers are quantitatively transformed to terminal N<sub>3</sub>Zn–OH units by treatment with tetrabutylammonium hydroxide to yield MFU-4l(OH) with a conserved framework structure.

After confirming the structure, Dincă and co-workers proceeded to probe the enzymatic reactivity of MFU-4l(OH). Considering that the essential function of CA is to catalyze the

reversible hydration of carbon dioxide and a critical step in this process is CO<sub>2</sub> insertion into the Zn–OH bond, the authors thus studied its CO<sub>2</sub> sorption behavior by collecting CO<sub>2</sub> sorption isotherms. To gain more insight into the framework-adsorbate interaction, they calculated the isosteric heat of adsorption ( $Q_{st}$ ) as a function of the amount of CO<sub>2</sub> adsorbed on the basis of the adsorption isotherms measured at three different temperatures (288, 298, and 308 K). Calculated with the virial equation, the  $Q_{st}$  at zero CO<sub>2</sub> coverage was 81 kJ mol<sup>-1</sup>, reflecting a strong chemisorption mechanism and agreeing with the reaction enthalpies determined for CO<sub>2</sub> fixation by transition-metal hydroxide complexes (49–61 kJ mol<sup>-1</sup>). With increasing coverage, the  $Q_{st}$  stayed relatively constant up to 0.5 equiv of CO<sub>2</sub> per SBU and then steadily decreased from 62 to 35 kJ mol<sup>-1</sup> for the second CO<sub>2</sub> equivalent and from 35 to 20 kJ mol<sup>-1</sup> for the third CO<sub>2</sub> equivalent. To reveal the underlying mechanism, the authors carried out quantum density functional theory computations to understand the enthalpies required for CO<sub>2</sub> insertion into different Zn–OH units. The trend of decreasing binding enthalpy along with the CO<sub>2</sub> adsorption is consistent with the experimental data. These results suggest that with the conversion of the highly basic –OH to weakly basic –OCO<sub>2</sub>H (Figure 1C), the nucleophilicity of the remaining Zn–OH sites within a given metal node are weakened, thereby resulting in decreased  $Q_{st}$  values. Given the significant uptake capacity (3.41 mmol g<sup>-1</sup> at 298 K) and limited energy cost required for regeneration, this material gives

great promise for CO<sub>2</sub> capture and sequestration.

To further prove the ability of MFU-4l(OH) to perform CA-like reactivity, the authors investigated the reversible hydration of CO<sub>2</sub> by studying the exchange of <sup>18</sup>O-labeled H<sub>2</sub>O with gaseous CO<sub>2</sub>. The time to reach an equilibrium mixture of the three possible CO<sub>2</sub> isotopologues (C<sup>16</sup>O<sub>2</sub>, C<sup>16,18</sup>O<sub>2</sub>, and C<sup>18</sup>O<sub>2</sub>) was significantly reduced from 10 to 5 hr after MFU-4l(OH) was introduced. Also, MFU-4l(OH) exhibited activity in the hydrolysis of 4-nitrophenyl acetate (4-NPA) with a 15% ± 2% conversion after 24 hr, in contrast with 1.7% ± 0.2% conversion of the blank control. These results thereby prove that the metal nodes of MFU-4l can be functionalized to serve as a high-fidelity biomimetic model of the CA active site.

This contribution demonstrates an elegant example of functionalizing a MOF metal node to mimic the activity of an enzyme. Facilitated by the modularity of MOFs and the diverse toolbox of synthetic modification techniques that they offer, it is conceivable that MOF-based materials show great potential in the field of biomimetic chemistry.<sup>9,10</sup> Taking inspiration from enzymes, it will be intriguing to see the advantages that MOFs can offer in advanced material design. As this paper shows, MOFs with enzyme-like active sites afford great opportunities to push the boundaries of numerous challenges faced nowadays, such as CO<sub>2</sub> capture and sequestration. With high structural fidelity and reactivity, MOFs hold potential for future under-

standing of enzyme chemistry and also the potential to perform enzyme-inspired reactions in stable frameworks. As more and more stable MOFs are discovered, researchers are beginning to tap into the potential of this class of material for industrially viable applications.

1. Schmid, A., Dordick, J.S., Hauer, B., Kiener, A., Wubbolts, M., and Witholt, B. (2001). Industrial biocatalysis today and tomorrow. *Nature* 409, 258–268.
2. Sanchez, C., Arribart, H., and Guille, M.M.G. (2005). Biomimetic and bioinspiration as tools for the design of innovative materials and systems. *Nat. Mater.* 4, 277–288.
3. Chen, Y., and Ma, S. (2016). Biomimetic catalysis of metal-organic frameworks. *Dalton Trans.* 45, 9744–9753.
4. Nath, I., Chakraborty, J., and Verpoort, F. (2016). Metal organic frameworks mimicking natural enzymes: a structural and functional analogy. *Chem. Soc. Rev.* 45, 4127–4170.
5. Doonan, C., Riccò, R., Liang, K., Bradshaw, D., and Falcaro, P. (2017). Metal-organic frameworks at the biointerface: synthetic strategies and applications. *Acc. Chem. Res.* 50, 1423–1432.
6. Zhou, H.-C., Long, J.R., and Yaghi, O.M. (2012). Introduction to metal-organic frameworks. *Chem. Rev.* 112, 673–674.
7. Parkin, G. (2004). Synthetic analogues relevant to the structure and function of zinc enzymes. *Chem. Rev.* 104, 699–767.
8. Wright, A.M., Wu, Z., Zhang, G., Mancuso, J.L., Comito, R.J., Day, R.W., Hendon, C.H., Miller, J.T., and Dincă, M. (2018). A structural mimic of carbonic anhydrase in a metal-organic framework. *Chem* 4, this issue, 2894–2901.
9. Jin, C., Zhang, S., Zhang, Z., and Chen, Y. (2018). Mimic carbonic anhydrase using metalorganic frameworks for CO<sub>2</sub> capture and conversion. *Inorg. Chem.* 57, 2169–2174.
10. Bien, C.E., Chen, K.K., Chien, S.-C., Reiner, B.R., Lin, L.-C., Wade, C.R., and Ho, W.S.W. (2018). Bioinspired metal-organic framework for trace CO<sub>2</sub> capture. *J. Am. Chem. Soc.* 140, 12662–12666.