

## A Catalyst that Efficiently Transforms Methane into Methanol at Room Temperature

*This report features the work of Sunney Chan and his co-workers published in Angew. Chem. Int. Ed. 52, 3731 (2013).*

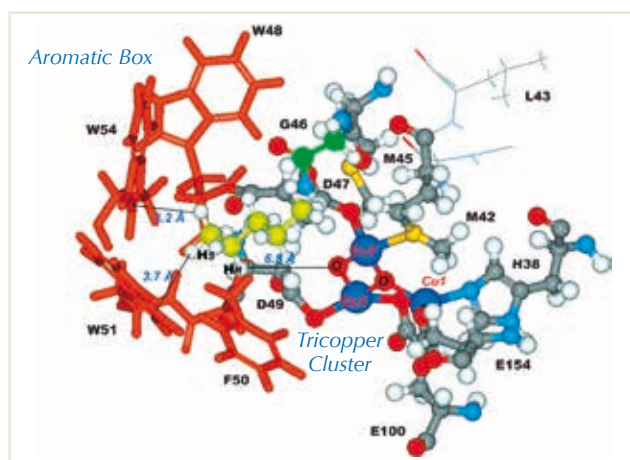
The planet has huge reserves of methane ( $\text{CH}_4$ ), which can be converted into methanol ( $\text{CH}_3\text{OH}$ ) to be used as an alternative fuel. Methanol is also an important feedstock for the production of many highly valued chemical products including formaldehyde, acetic acid, and plastics, among many. In addition, it is readily converted to  $\text{H}_2$ , the vital fuel in a hydrogen economy. Thus there is currently considerable interest in developing a laboratory catalyst suitable for the conversion of methane to methanol on an industrial scale.

A research team led by Sunney Chan and Steve Yu, working together in the Institute of Chemistry at Academia Sinica, has recently succeeded in developing the first efficient catalyst to convert  $\text{CH}_4$  into  $\text{CH}_3\text{OH}$  under ambient conditions. This chemistry is extremely difficult to carry out in the laboratory especially at room temperature. The C–H bond in  $\text{CH}_4$  is extremely inert due to its high bond-dissociation energy (105 kcal/mole).<sup>1</sup> In addition, the product  $\text{CH}_3\text{OH}$  is prone to further oxidation to form other products.<sup>1</sup>

In developing the catalyst, the Chan/Yu team has learned from microbes to understand how Mother Nature uses methanotrophic bacteria to convert  $\text{CH}_4$  into  $\text{CH}_3\text{OH}$ . Methanotrophs are prokaryotes that are able to metabolize methane as their only source of carbon and energy. Under aerobic conditions, they combine  $\text{O}_2$  and  $\text{CH}_4$  to form formaldehyde, which is then incorporated into organic compounds to survive. In this metabolic pathway,  $\text{CH}_4$  is first converted into  $\text{CH}_3\text{OH}$  by an enzyme called the particulate methane monooxygenase (pMMO). This enzyme accomplishes this chemistry with high efficiency, converting one  $\text{CH}_4$  molecule to one  $\text{CH}_3\text{OH}$  per sec.<sup>1</sup> These microbes are found mostly in soils, and are especially common near environments where  $\text{CH}_4$  is produced. Their habitats include oceans, mud, marshes, under-

ground environments, soils, rice paddies and landfills. Methanotrophic bacteria are also of special interest to researchers studying global warming, as they are significant in the global methane budget.

To solve the puzzle of how the pMMO mediates the efficient oxidation of methane to methanol, the Chan/Yu laboratories have had to over-produce the protein in the bacterial cells, isolate the protein from the cell membranes, purify the protein to homogeneity, and then characterize the purified protein by a barrage of biochemical and biophysical methods, including electron paramagnetic resonance spectroscopy and X-ray absorption spectroscopy. From these studies,<sup>1</sup> they discovered that the catalytic site of the enzyme consists of a unique  $\text{Cu}^I\text{Cu}^I\text{Cu}^I$  tricopper cluster. They synthesized the peptide that lines the putative catalytic site and showed that it is capable of sequestering a  $\text{Cu}^I\text{Cu}^I\text{Cu}^I$  tricopper cluster, which, upon activation with  $\text{O}_2$ , can mediate oxidation of  $\text{CH}_4$  to  $\text{CH}_3\text{OH}$ .<sup>2</sup> The redox chemistry and the ligand structures of both the  $\text{Cu}^I\text{Cu}^I\text{Cu}^I$  and  $\text{Cu}^{II}\text{Cu}^{II}\text{Cu}^{II}$

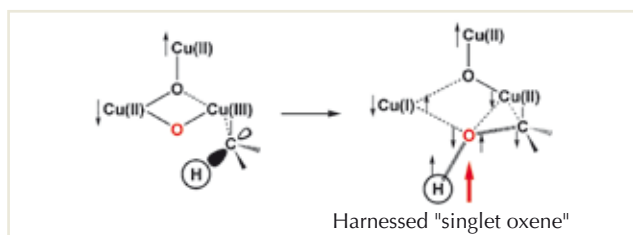


**Fig. 1:** Schematic representation of the catalytic site of pMMO, in which the tricopper cluster (copper atoms are highlighted in blue) in the protein structure is shown in close proximity to a pentane molecule (yellow) as the substrate in the alkane binding pocket. (Reproduced from Ref. 1)

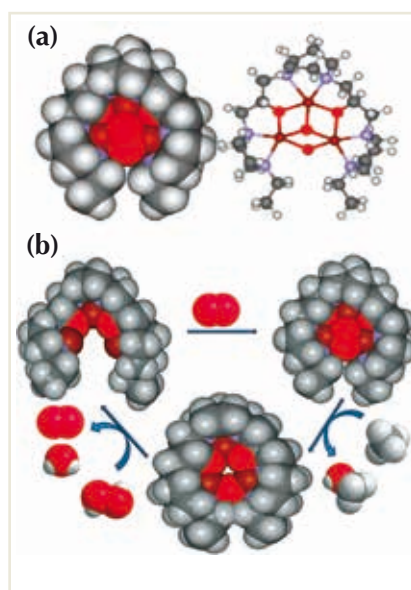
peptide complexes have been determined by EXAFS studies carried out at **BL17C1** of the TLS. The proposed structure of the putative catalytic site containing the activated tricopper cluster in the enzyme is depicted in Fig. 1, together with a molecule of pentane encapsulated in the hydrocarbon binding-pocket of the enzyme. Pentane is the longest straight-chain alkane that can be hydroxylated by the enzyme.

Density functional theory calculations show that the activated tricopper cluster can harness a “singlet oxene” that can be transferred to the hydrocarbon substrate for direct concerted insertion across the C–H bond when the alkane forms a transient complex with the tricopper cluster.<sup>1</sup> The mechanism of the “singlet oxene” transfer is depicted in Fig. 2. The deployment of a tricopper cluster to harness a “singlet oxene” is novel chemistry. The “singlet oxene” is the strongest oxidizing agent known in chemistry.

Armed with these insights, Chan and Yu have now developed a biomimetic catalyst that can mediate the efficient transformation of  $\text{CH}_4$  into  $\text{CH}_3\text{OH}$  at room temperature. They have discovered that the tricopper complex  $[\text{Cu}^{\text{I}}\text{Cu}^{\text{I}}\text{Cu}^{\text{I}}(\mathbf{7-N-Etppz})]^{1+}$ , where **7-N-Etppz** stands for the organic ligand 3,3'-(1,4-diazepane-1,4-diyl)bis[1-(4-ethyl piperazine-1-yl)propan-2-ol] mediates the facile conversion of  $\text{CH}_4$  to  $\text{CH}_3\text{OH}$  upon activation of the catalyst by  $\text{O}_2$ . The structure of the activated tricopper catalyst is shown in Fig. 3(a) and the catalytic cycle for the selective oxidation of  $\text{CH}_4$  to  $\text{CH}_3\text{OH}$  is depicted in Fig. 3(b).<sup>3</sup> Here, the  $[\text{Cu}^{\text{I}}\text{Cu}^{\text{I}}\text{Cu}^{\text{I}}(\mathbf{7-N-Etppz})]^{1+}$  complex is acti-



**Fig. 2:** Details of the adiabatic “singlet oxene” transfer from a dioxygen activated trinuclear copper cluster to  $\text{CH}_4$  to form the transition state.  $\uparrow$  and  $\downarrow$  denote the “up” and “down” directions of the unpaired electron spins. (Reproduced from Ref. 1)



**Fig. 3:** Top: Space-filling model (left) and ball-and-stick model (right) of the optimized structure of  $[\text{Cu}^{\text{I}}\text{Cu}^{\text{II}}(\mu\text{-O})_2\text{Cu}^{\text{III}}(\mathbf{7-N-Etppz})]^{1+}$  showing the funnel-like opening or cleft at the bottom for a hydrocarbon substrate to access the “hot oxene”. Color code- white: hydrogen; grey: carbon; blue: nitrogen; red: oxygen; brown: copper (Reproduced from Ref. 2). Bottom: The catalytic cycle for the conversion of  $\text{CH}_4$  into  $\text{CH}_3\text{OH}$  mediated by the tricopper catalyst (Reproduced from Ref. 3).

vated by  $\text{O}_2$  to the  $[\text{Cu}^{\text{I}}\text{Cu}^{\text{II}}(\mu\text{-O})_2\text{Cu}^{\text{III}}(\mathbf{7-N-Etppz})]^{1+}$  species, and the harnessed “singlet oxene” is then transferred upon formation of a weak transient complex between the activated cluster and the  $\text{CH}_4$  substrate. Following the reaction, the “spent” catalyst is re-reduced by a molecule of  $\text{H}_2\text{O}_2$  to regenerate the catalyst to complete the catalytic cycle.

The  $[\text{Cu}^{\text{I}}\text{Cu}^{\text{I}}\text{Cu}^{\text{I}}(\mathbf{7-N-Etppz})]^{1+}$  complex can also mediate the oxidation of other small alkanes to their corresponding alcohols and aldehydes/ketones with high efficiencies near room temperature.<sup>3</sup> Significantly, for methane, ethane and propane, the three major components of natural gas, are oxidized only to methanol, ethanol and 2-propanol, respectively. There is no evidence for any over-oxidation of these alkanes during the catalytic turnover. The propensity to over-oxidation is one of the greatest challenges in the design of a catalyst for the conversion of  $\text{CH}_4$  into  $\text{CH}_3\text{OH}$ . Thus, Chan and Yu have achieved one of the most significant objectives in the development of a catalytic system for methane oxidation.

## References

1. P. P.-Y. Chen, P. Nagababu, S. S.-F. Yu, and S. I. Chan, *ChemCatChem* **6**, 429 (2014).
2. S. I. Chan, Y. J. Lu, P. Nagababu, S. Maji, M. C. Hung, M. M. Lee, I. J. Hsu, P. D. Minh, J. C. H. Lai, K. Y. Ng, S. Ramalingam, S. S.-F. Yu, and M. K. Chan, *Angew. Chem. Int. Ed.* **52**, 3731 (2013).
3. P. Nagababu, S. S.-F. Yu, S. Maji, R. Ramu, and S. I. Chan, *Catal. Sci. Technol.* **4**, 930 (2014).