Role of Metal Identity and Speciation in the Low-Temperature Oxidation of Methane over Tri-Metal Oxo Clusters

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Abstract

Clarity as to the role of metal identity and oxidation state in effecting redox and acid-catalyzed turnovers is oftentimes precluded by a high degree of heterogeneity in site speciation, a limitation that can be overcome through the use of well-defined polymetal clusters hosted by metal organic framework materials- accomplished in the present case using MIL-100(M) for the low temperature oxidation of methane with N2O. Transient kinetic data point to a) methoxy species mediating methane conversion, b) partial and deep oxidation occurring over metal sites distinct in oxidation state, c) chromium clusters amplifying the propensity toward C-C bond formation, and d) the relative velocity of propagation of water and methanol concentration fronts playing a determinative role in maximizing C2 oxygenate selectivity. The study captures the utility of using classes of materials inherently endowed with a high level of definition and uniformity in advancing the elucidation of structure-catalytic property relationships.

1. Introduction

The selective, low-temperature oxidation of methane to methanol, if successfully accomplished, could enable valorization of vast reserves of shale gas resources becoming increasingly abundant in the United States and around the world. ¹⁻³ High-valent metal-oxo complexes serve as promising active centers for low-temperature methane oxidation, and are exploited in a variety of biological and synthetic systems;⁴⁻⁸ for instance, iron(IV)-oxo centers have been long hypothesized as the key oxidizing species in non-heme biological complexes including R2 proteins of ribonucleotide reductase (RNR R2), Fe²⁺/ α -ketoglutarate (α KG)-dependent hydroxylates, and soluble methane monooxygenase (sMMO) enzymes.⁹⁻¹⁴ Efforts aimed at investigating such active centers have for the most part been focused on iron-zeolites in the heterogeneous catalysis literature¹⁵⁻¹⁹ and homogenous complexes in the bioinorganic chemistry literature,²⁰⁻²³ with both classes of materials exhibiting unique limitations with respect to low temperature methane oxidation. Homogeneous complexes, on one hand, often display a propensity towards polynuclear aggregation, thereby limiting somewhat their use in catalysis applications.²⁴⁻²⁸ Iron-based zeolites, on the other hand, while ideal for investigating iron clusters that do not evolve significantly under reaction conditions, exhibit active site heterogeneity not only greater in degree than that exhibited by homogeneous complexes, but also to an extent that varies significantly with synthesis protocol, thermal treatment, and iron loading.²⁹⁻³¹

Metal-organic framework materials (MOFs) potentially offer a solution to the challenge of synthesizing and evaluating materials that carry well-defined, structurally uniform metal-oxo moieties that remain isolated in nature subsequent to their involvement in catalytic redox cycles, with several copper and iron-containing MOFs having been evaluated for the oxidation of light alkanes including methane,^{32–35} ethane,^{36–38} and propane.³⁹ Specifically, MIL-100 (MIL =*Materials of Institut Lavoisier*) is a MOF that exhibits interesting properties in the partial oxidation of light alkanes.^{35,39–41} First discovered by Gérard Férey and coworkers, MIL-100 is comprised of trimetallic clusters [(M(III)₃(μ_3 -O)] coordinated by trimesate linkers to form a porous structure featuring an MTN (Mobile Thirty Nine) topology (Scheme 1a).⁴² Removal of terminal ligands (H₂O or X⁻) through thermal activation under inert or vacuum at temperatures below 523 K (Scheme 1b) creates unsaturated open-metal sites over mixed valence nodes $[(M(II)M(III)_2(\mu_3-O)]$.^{43–45}The propensity of these nodes to convert methane to methanol at low temperatures (423

Scheme 1. (a) Structure of MIL-100 comprised of trimesic acid linkers and μ_3 -oxo centered trimer nodes. (b) Formation of M^{2+} and M^{3+} open-metal sites in MIL-100 through thermal activation resulting in the elimination of anionic ligands and coordinated water molecules, respectively.



- 473 K) and ambient pressures has been previously demonstrated,^{39,40} including a prior report from our group evidencing participation of every single MIL-100 tri-iron node towards methanol formation,³⁵ unlike iron-zeolites that typically carry *distributions* of active and inactive multinuclear iron centers.⁴⁶⁻⁴⁹ In this study, we use a suite of spectroscopic, transient kinetic, and site titration tools to relate metal oxidation state to reactive function. Specifically, the role of Fe²⁺ and Fe³⁺ sites in methanol and CO₂ formation are identified. Altering the identity of the metal from iron to chromium enables C-C bond formation events that appear to involve methoxy intermediates that also mediate methanol formation over both MIL-100(M) variants. To this end, we elucidate in Section 3.1 the identity of sites involved in CO₂ and methanol formation,

identify in Section 3.2 the role of methoxy intermediates, demonstrate the propensity towards and methods for controlling the prevalence of C-C bond formation over MIL-100(Cr) in Section 3.3, before clarifying the diversity of functionality of Fe³⁺-methoxies in Section 3.4 The study captures how precise control over metal identity and oxidation state, combined with manipulation of the relative velocity of water and methanol concentration fronts, enables control not only over the selectivity towards desired partial oxidation products such as methanol (versus CO_2) but also that towards C2 oxygenates (over C1 oxygenates).

2. Materials and Methods

2.1. Synthesis and characterization

MIL-100(Fe) and MIL-100(Cr) were synthesized according to previously reported protocols^{50,51} that are described in detail in Sections S1.1 and S1.2. of the SI. Comparison of X-ray diffraction patterns, nitrogen physisorption isotherms, and thermogravimetric analysis profiles confirm the crystal structure, porosity, and composition, respectively, of these materials as being consistent with previous reports (Figure S1 and S2).^{50,51} Infrared (IR) spectroscopy measurements were conducted to track the evolution of H₂O and OH⁻ coordinated species in MIL-100(Fe) and MIL-100(Cr) to estimate M^{2+}/M^{3+} open-metal site densities under various thermal activation conditions (as described in detail in Section S1.6 of the SI). Fe²⁺ and Fe³⁺ open-metal site densities were quantified in-situ using a combination of breakthrough measurements with NO (0.5 kPa, 423 K) and D₂O (0.9 kPa, 373 K), as described in Sections 2.4 and 2.5 of the SI, respectively.

2.2. Methane oxidation experiments

Details of methane oxidation reaction experiments are described in Section S1.4 of the SI. Briefly, pretreated MIL-100 samples (423 - 523 K, 12 h, He flow (50 mL min⁻¹) or vacuum (P < 1 x 10⁻⁴ bar)) were exposed to CH₄/N₂O reactant mixtures at 423 - 473 K with gas-phase product and reactant concentrations determined using a gas chromatograph (Agilent 7890 B). Following reaction, water vapor at various partial pressures (0.35 - 1.1 kPa) and molar flow rates ($1.54 - 4.61 \times 10^{-6}$ mol s⁻¹) were introduced to extract surface-bound intermediates at temperatures between 373 and 473 K, and products formed were measured using an online mass spectrometer (MKS Cirrus 2).

2.3. In-situ titrations

Titration experiments with NO (10 wt.% NO, balance N₂, Matheson, Research Purity) and H₂O (deionized, 18.3 MΩ) were conducted at 423 K under constant reaction conditions: 14.5 kPa N₂O, 1.5 kPa CH₄, t = 2 h. For NO titration experiments, NO was fed over MIL-100(Fe) prior to the introduction of CH₄ and N₂O due to the significant time it takes for NO to break through the MOF bed in comparison to the reactants (Section S2.6, SI). Under titrant co-feeds, inert carrier gas (He, Matheson, Ultra High Purity) concentrations were reduced to maintain constant reactant partial pressures. Total quantities of NO and H₂O adsorbed by MIL-100 were estimated through breakthrough curves measured using an online mass spectrometer (MKS Cirrus 2) at the outlet of the bed. Molar flow rates were calibrated with respect to those of argon (internal standard) under the assumption that no argon was adsorbed by the sample.

3. Results and Discussion

3.1. Active site requirements for methanol and CO_2 formation

We previously reported the oxidation of methane to methanol and CO_2 at low temperatures (423 – 483 K) and sub-ambient pressures over tri-iron oxo clusters hosted by MIL-100(Fe) nodes.³⁵ Co-feeding N₂O and methane at 473 K over MIL-100(Fe) activated at 523 K resulted in transient dinitrogen formation rates that decrease asymptotically toward a constant value and CO_2 formation

rates that appear to be invariant in time (Figure 1). Extraction with water vapor (0.35 kPa, 473 K) subsequent to exposure to methane and N₂O resulted in the formation of methanol, the cumulative yield of which asymptotically approaches a maximum value with reaction time (Figure 1). Reported N₂ formation rates are consistent with those expected based on the combination of methane oxidation to methanol, CO₂ and water based on the reaction stoichiometry (N₂O + CH₄ - N₂ + CH₃OH; 4N₂O + CH₄ - 4N₂ + CO₂

+ 2H₂O), as reflected by the close correspondence between measured cumulative nitrogen yields and those estimated from reaction stoichiometry (Figure 1). The maximum cumulative methanol yield measured corresponds to the theoretical maximum density of Fe²⁺sites in MIL-100 (0.33 mol Fe²⁺/mol total Fe). Furthermore, Fe²⁺ site densities estimated from FTIR signatures of either terminal hydroxyl ligands or NO coordinated to Fe²⁺ sites created upon hydroxyl removal serve as proxies for cumulative methanol formation, lending credence to the possible sole involvement of Fe²⁺ sites in methanol formation.³⁵



Figure 1. Cumulative moles of N_2 , CO_2 , and CH_3OH formed as a function of time of exposure to CH_4 and N_2O . The quantity of CH_3OH reported is that formed upon extraction with water subsequent to CH_4/N_2O exposure. The estimated quantity of N_2 formed was determined by the balance of CH_3OH and CO_2 formed $[(mol N_2) = (mol CH_3OH) + 4(mol CO_2)]$ Reaction conditions: 2.9 kPa N_2O , 1.5 kPa CH_4 , 0.35 kPa H_2O , 473 K, MIL-100(Fe) activated at 523 K.

The invariance in CO_2 formation rates with time despite the consumption of Fe^{2+} sites converting methane to methanol indicates that Fe^{2+} site densities that allow for the rigorous normalization of methanol formation, do not do so for CO_2 formation, and suggests an independence between sites responsible for the formation of these two products. Moreover, unlike methanol formation, which can be completely inhibited by the presence of gas phase NO under reaction conditions, the formation of CO_2 is unaffected by the presence of NO, as reflected by the insensitivity of cumulative CO_2 formation to the presence of NO co-feeds (Figure 2a). Reported cumulative moles of CO_2 formed are corrected for those measured when NO was flown over MIL-100(Fe) in the absence of methane and N_2O (0.0035 mol (mol total Fe)⁻¹). Such NO-induced oxidation (presumably of the MIL-100 framework) accounts accurately for the slight increase in CO_2 formation upon introduction of NO with methane and N_2O (0.0039 mol (mol total Fe)⁻¹, Table S4), and suggests that linker oxidation rates are unaffected by the presence of methane and N_2O . The insensitivity in cumulative CO_2 formation rates to Fe²⁺ site densities both in the presence and absence of NO suggest that a significant fraction of CO_2 formation may occur over a distinct set of sites compared to those identified for methanol formation.

Given the near complete absence of NO adsorption onto Fe^{3+} sites under reaction conditions and the insensitivity of CO_2 formation rates to the presence of NO in the gas phase, their involvement in CO_2 formation warrants further evaluation- a question that is challenging to definitively address in the absence of titrants that bind exclusively to Fe^{3+} sites (and not Fe^{2+} sites). A clue as to the involvement of Fe^{3+} sites in CO_2 formation is provided by water titrations $(0.9 \text{ kPa H}_2\text{O} \text{ at } 423 \text{ K})$ that bind unselectively to open-metal sites regardless of their oxidation state, as indicated by the adsorption of one mole water per mol iron under conditions of interest (Figure S8). Whereas co-feeding NO eliminates (solely) CH₃OH formation, introduction of H_2O with methane and N_2O (14.5 kPa N_2O , 1.5 kPa CH_4 , 0.9 kPa H_2O) results in the complete elimination of both oxidation products (Figure 2a). Additionally, the presence of 0.5 kPa NO in the gas phase causes the introduction of increasing H_2O partial pressures (0.1 - 0.9 kPa) to result in a systematic increase in the total quantity of water adsorbed, and a concurrent linear decrease in cumulative moles of CO_2 formed with increasing amount of water adsorbed (Figure 2b). The linear relationship between the cumulative moles of CO_2 formed and those of water adsorbed reflects a constant ratio between the number of sites that adsorb water and those eliminated from participation in CO_2 formation. Moreover, the quantity of water adsorption required to completely suppress CO_2 formation was found to be 0.62 mol (total mol $Fe)^{-1}$ - a value approximately equal to the concentration of Fe^{3+} open-metal sites (0.65 mol (total mol Fe)⁻¹) measured independently using D_2O adsorption measurements (Section S2.5, SI).



Figure 2. (a) Cumulative moles of methanol (left axis) and CO₂ (right axis) formed per total Fe in the absence of any titrant and in the presence of NO (0.5 kPa) or H₂O (0.9 kPa). (b) Under 0.5 kPa NO, the quantity of H₂O adsorbed in MIL-100(Fe) over a range of partial pressures (0.1 - 0.9 kPa) and the cumulative moles of CO₂ formed per total Fe under that condition. Reaction conditions: 423 K, 14.5 kPa N₂O, 1.5 kPa CH₄, t = 2 h, activated at 523 K for 12 h in He.

Thermal treatment protocols can be used to access increasing densities of Fe^{2+} and Fe^{3+} sites, $^{35, 43, 52}$ with activation temperatures below 423 K yielding a majority of Fe^{3+} sites, and those above 423 K resulting in the formation of Fe^{2+} sites in addition to Fe^{3+} sites (Table S3). Cumulative CO₂ yields normalized by the density of Fe^{3+} sites remain nearly invariant in activation temperature, unlike those normalized by total iron content which increase monotonically with activation temperature (Figure 3), consistent with the involvement of the former in CO_2 formation. Also consistent with the sole involvement of Fe^{3+} sites is the monotonically decreasing trend of CO_2 formation rates per Fe²⁺ site with activation temperature, expected to result from greater relative contributions of Fe^{3+} sites to the total open-metal site density at higher temperatures (Figure S9). Overall, CO_2 cumulative yields that increase linearly with time and are unaffected by decreasing Fe^{2+} site densities, the insensitivity of CO₂ formation rates to NO pressure, a linear correlation between the amount of water adsorbed in the presence of NO and cumulative CO₂ yields, the precise correspondence between the moles of water required to saturate Fe^{3+} sites and those required for the complete elimination of CO_2 formation, and the invariance in Fe^{3+} -normalized cumulative CO_2 yields with increasing thermal activation temperature are all consistent with and suggestive of the involvement of Fe^{3+} sites in CO₂ formation, even though these data do not help definitively exclude the possibility that a minute amount of extraframework iron may be responsible for the same.



Figure 3. Cumulative moles of CO₂ formed normalized by the total iron content (left axis) and per Fe³⁺ open-metal site (right axis) with increasing activation temperature (423 - 523 K). Reaction conditions: 473 K, 14.5 kPa N₂O, 1.5 kPa CH₄, t = 2 h, activated at temperature for 12 h in He.

Gagliardi, Snurr, and co-workers have reported density functional theory (DFT)-derived energy profiles for the decomposition of N_2O over M^{2+} sites to form M(IV)=O species;^{39,40,53} crucially, calculations reported

by Barona and Snurr suggest the potential for M^{3+} coordinatively unsaturated sites situated in trimeric MOF nodes to participate in methane oxidation with N₂O.⁵⁴ For example, a V³⁺ open-metal site in the $(Ni^{2+})(V^{3+})_2$ mixed-metal node was proposed to be oxidized by N₂O to $Ni^{2+}(V^{4+}=O)V^{4+}$, with both of the trivalent vanadium centers donating electrons to form the oxo intermediate. N₂O activation barriers over Fe³⁺ open-metal sites in $[(Cr^{2+})(Fe^{3+})_2]$ and $[(Mn^{2+})(Fe^{3+})_2]$ mixed-metal nodes (144 and 146 kJ mol⁻¹, respectively) were found to be comparable to those predicted for Fe²⁺ open-metal sites on an $(Fe^{2+})(Fe^{3+})_2$ node (146 kJ mol⁻¹). The involvement of Fe³⁺ sites in methane oxidation may proceed through the involvement of metal-oxo bond formation steps of such a nature, and a fuller understanding of these steps may require knowledge of changes in formal oxidation states over the entire trimer rather than merely one of three metal atoms constituting the node.

3.2. The key role of methoxy intermediates in methane conversion

The absence of gas phase methanol at the reactor outlet during both the methane-nitrous oxide co-feed step as well as the ensuing purge step under inert, but its detection upon exposing the sample to water vapor during the extraction step suggests one of two possibilities: a) water displaces adsorbed methanol through competitive adsorption, or b) reacts with a persistent intermediate formed upon exposure to methane and N_2O to form gas phase methanol. Exposure to D_2O (as opposed to H_2O) allows for a differentiation between these two scenarios. Whereas the displacement of adsorbed methanol by water should result in the exclusive detection of non-deuterated methanol, incorporation of deuterium into the methanol product would be indicative of the formation of a persistent intermediate that undergoes steps involving the exchange of deuterium from water. Exposure to D_2O was found to result exclusively in the formation of monodeuteromethanol (Figure 4a), consistent with the formation of methoxy intermediates that then undergo reaction with water to form methanol and reform the hydroxyl anion that was eliminated to create the Fe^{2+} site in the first place. The fraction of mono-deuteromethanol in the product tracks with the fraction of D_2O in H_2O - D_2O mixtures that the methoxy-covered surface is exposed to (Figure 4b), suggesting a lack of preferential incorporation of hydrogen versus deuterium into the methanol product. Exposure to $H_2^{18}O$ yielded exclusively $CH_3^{16}OH$ (Figure 4c), consistent with the formation of methoxy intermediates that desorb subsequent to bond formation between methoxy oxygens and hydrogens/deuteriums in water. These data suggest that a significant fraction of the methane converted form methoxy intermediates which are then extracted using water vapor, and are inconsistent with the formation of adsorbed methanol that is subsequently displaced by water.



Figure 4. (a) Molar formation rate (per total Fe) of CH_3OH and CH_3OD formed over MIL-100(Fe) when exposed to D_2O at 473 K following reaction. (b) Effect of the molar ratio of H_2O and D_2O fed during the product extraction step on the relative amount of CH_3OH and CH_3OD formed. (c) Molar formation rate (per total Fe) of $CH_3^{16}OH$ and $CH_3^{18}OH$ over MIL-100(Fe) when exposed to $H_2^{18}O$ at 473 K following reaction. (1.6 kPa N₂O, 1.5 kPa CH₄, 473 K, 2 h). Figure 4b reproduced from ref. ³⁵ Copyright © 2020 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.

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Reaction with water to form methanol from intermediates that are not desorbed from the surface in the absence of water mirrors several observations reported in prior literature. Ethane oxidation over MOF-74(Mg,Fe) to produce ethanol, acetaldehyde, and diethyl ether required extraction with CD₃CN following reaction at 348 K.³⁶ Propane/ethane oxidation over MIL-100(Fe) also required oxygenated products to be extracted with D_2O , with only unsaturated ethene/propene products desorbing into the gas phase in the absence of D_2O .³⁹ DFT calculations reported by Vitillo *et al.* evaluating the radical rebound mechanism for methanol formation suggest that the step involving formation of the Fe(IV)=O intermediate over MIL-100(Fe) carries the highest activation barrier (140.5 kJ mol⁻¹).⁴⁰ The authors suggest that alcohol desorption may not readily occur under reaction conditions due to the high activation barrier for the desorption for methanol (91.5 kJ mol⁻¹) in comparison to the heat of adsorption of N_2O (30 kJ mol⁻¹). A competing pathway to radical rebound to form the surface bound methanol product is one in which the radical dissociates from the active center.^{55,56} The activation energy for radical desorption from Fe nodes in MIL-100(Fe) MOFs was predicted to be only slightly greater ($\sim 5 \text{ kJ mol}^{-1}$ greater) than the barrier for radical rebound.⁴⁰ We note in this context that experimental evidence for *catalytic* methane hydroxylation over MIL-100(Fe) has not yet been reported in the literature. Though methoxy intermediates are identified in our study as the predominant species formed prior to exposure to water vapor, the identity of elementary steps that form them remain unclear, and the possibility of minor quantities of methanol being formed is challenging to disprove given the plausibility of methanol reacting with open-metal iron sites, as demonstrated in the discussion that follows.

To test for the plausibility of methoxy formation mediated by either adsorbed or gas phase methanol, thermally-activated MIL-100(Fe) was first exposed to CH_3OH at 373 K, purged for 6 h under inert flow at 473 K to remove excess CH_3OH , and then exposed to D_2O . 0.23 mol CH_3OD (mol Fe)⁻¹ were measured upon introduction of D_2O subsequent to exposure to methanol, a value coinciding closely with that formed following reaction with methane and N₂O (0.27 mol CH₃OD (mol Fe)⁻¹)- Figure 5- evidencing the plausibility of methoxy formation through methanol dissociation over Fe^{2+} sites. The methanol dissociation observed is analogous to water reacting with open-metal sites to reform hydroxyl anions that have to be eliminated during thermal activations steps in MIL-100(Fe) (Figure S11, SI), as also reported previously over Cr^{2+} sites in MIL-100(Cr).⁴⁵ The susceptibility of methanol towards dissociation over Fe^{2+} sites suggests that the formation of methanol intermediates in our experiments cannot be excluded. Regardless of the identity of steps mediating methoxy formation, its stoichiometric formation exclusively over Fe^{2+} sites appears to precede methanol formation upon extraction with water vapor. A 1:1 correspondence between methoxy concentrations and Fe^{2+} site densities across a range of thermal activation conditions³⁵ suggests that methoxy formation involves the participation of only one active center, and contrasts with prior reports for ironexchanged zeolites that propose the involvement of two active ' α -oxygen' sites per methoxy formed (CH₄ + $2(O)_{\alpha} - (OH)_{\alpha} + (OCH_3)_{\alpha}).^{57,58}$



Figure 5. Molar flow rate (per total Fe) of CH_3OD when D_2O (0.4 kPa) is introduced after the following procedures: (Top) MIL-100(Fe) exposed to CH_3OH for 1 h at 373 K and then purged with He for 6 h at 473 K; (Bottom) following exposure to CH_4 and N_2O . Reaction conditions: 473 K, 1.6 kPa N_2O , 1.5 kPa CH_4 , 2 h.

3.3. Manipulating methoxy reactivity by controlling metal identity

Implicit in the 1:1 correspondence between Fe^{2+} site densities and the number of moles of monodeuteromethanol is the lack of secondary reactions between methoxy intermediates and gas phase methanol formed in primary reactions. Over and above this correspondence between active site densities and methanol yield, the absence of C2 oxygenates in the product stream and the fact that all the methane converted can be accounted for (within error) as methanol formed suggests that C2 intermediates, if formed over the MIL-100(Fe) surface under the conditions reported here thus far, may account for a minor fraction of converted methane. Extraction of intermediates formed under identical conditions by methane and N₂O over MIL-100(Cr), however, provides (in addition to the formation of methanol) significant yields of acetaldehyde (fractional molar selectivity = 0.81, Figure 6a).C3CHmeImplicit RecationRe Analogous to the case of tri-iron clusters, moles of methane converted over MIL-100(Cr) track with M²⁺ site densities (Figure 6b) estimated using infrared peak areas corresponding to the hydroxyl anion (Figure S12), pointing to their sole involvement in C-H activation. Cumulative moles of methane reacted per mole Cr^{3+} do not remain invariant in activation temperature but instead increase with the latter (Figure S13, SI) due to the higher Cr^{2+}/Cr^{3+} site ratios and the associated lower inactive open-metal site fractions made available through thermal activation at higher temperatures. M^{2+} sites therefore participate in the activation of methane over both the iron and chromium variants of MIL-100(M). Although Cr-NO interactions are significantly stronger over Cr^{2+} sites compared to Cr^{3+} sites, as shown using NO adsorption measurements at 303 K reported in our previous work,⁴⁵ in contrast with MIL-100(Fe), insignificant NO adsorption occurs onto Cr^{2+} open-metal sites at reaction temperatures (423 – 473 K), as indicated by NO adsorption breakthrough and IR spectroscopy measurements (Section S2.14, SI). We therefore rely solely on the correspondence between product yields and Cr^{2+} open-metal site densities to suggest their involvement in methoxy formation, unlike the case of MIL-100(Fe) in which in-situ titrations with NO provided additional corroborating evidence of the same.



Figure 6. (a) Fractional selectivity for oxygenated products formed during product extraction (473 K, 0.35 kPa H₂O, 1.54 x 10⁻⁶ mol s⁻¹) and the quantity of methane reacted (per total mol M) for MIL-100(Fe) and MIL-100(Cr) activated at 523 K under He flow and in vacuum, respectively. (Reaction conditions: 473 K, 2.9 kPa N₂O, 1.5 kPa CH₄, 2 h). (b) Cr²⁺ open-metal site densities estimated from IR spectroscopy measurements at various activation conditions and the corresponding cumulative moles of CH₄ reacted normalized by the Cr²⁺ open-metal site density (Reaction conditions: 423 K, 14.5 kPa N₂O, 1.5 kPa CH₄, 2 h).

We hypothesize that secondary reactions of methoxy intermediates with gas phase methanol are responsible for acetaldehyde formation. The presence of these secondary reactions prevent the use of D₂O for evidencing the prevalence of methoxy intermediates over MIL-100(Cr) upon exposure to methane and N₂O. Instead, the prevalence of these secondary reactions can be verified through extraction with 0.12 kPa methanol at 373 K which leads to the formation, exclusively, of ethanol in both MIL-100(Fe) and MIL-100(Cr) (Figure 7), with the moles of ethanol formed approximating to the M^{2+} site density for both materials (Table S6, SI). This result is consistent with the same methoxy-covered surface being prevalent in both MIL-100(M) variants following oxidation of CH₄, and product distributions detected upon exposure to water vapor being dependent on the differing propensities of Fe and Cr-methoxy intermediates to undergo C-C bond formation steps. It also appears that whereas carbon-carbon bond formation is not predicated on the presence of water vapor, it seems to be necessary for the formation of acetaldehyde (as opposed to ethanol) in MIL-100(Cr), as indicated by the observation of methanol and acetaldehyde as products under aqueous extraction conditions (Figure 6a). Both water and methanol appear to be necessary for acetaldehyde formation, as evident in experiments involving extraction using equimolar feeds at 373 K. As a reference condition, a temperature of 373 K and a water partial pressure of 0.12 kPa were chosen for the reason that significant water coverages are attained (0.42 mol H_2O mol Cr^{-1}) in the absence of measurable amounts of methanol or acetaldehyde formation (Figure 8a and Table 1). Co-feeding equimolar mixtures of methanol and water (0.12 kPa each) under these conditions leads to the formation of 0.93 moles acetaldehyde per mole methane reacted (or equivalently, per mol methoxy formed), evidencing near-complete coupling of methoxies with gas phase methanol. These results suggest that although methoxies can react with methanol in the absence of significant partial pressures of water, the presence of water is necessary for the production of acetaldehyde, rather than ethanol, as the C2 product, and point to water playing a role in acetaldehyde formation over and above (and may be even independent of) their involvement in primary reaction steps that lead to the formation of gas-phase methanol.



Figure 7. Molar flow rates of CH₃OH and C₂H₅OH when CH₃OH (0.12 kPa) is fed after CH₄ oxidation at 373 K over (a) MIL-100(Cr) and (b) MIL-100(Fe). (Reaction conditions: 473 K, 2.9 kPa N₂O, 1.5 kPa CH₄, 2 h, MIL-100(Fe) activated at 473 K under inert flow, MIL-100(Cr) activated at 523 K in vacuum).



Figure 8. Molar flow rates of CH₃OH, H₂O, and C₂H₄O at the reactor outlet as a function of time when either (a) 0.12 kPa H₂O or (b) 0.12 kPa H₂O and 0.12 kPa CH₃OH are fed over MIL-100(Cr) at 373 K following the oxidation of CH₄ (reaction conditions: 473 K, 2.9 kPa N₂O, 1.5 kPa CH₄, 2 h, activated at 523 K in He for 12 h).

Table 1. Comparison of the cumulative moles of CH_4 reacted and C_2H_4O formed over MIL-100(Cr) when the product extraction step is conducted under different pressures of H_2O and CH_3OH at 373 K. C_2H_4O to methoxy ratios are determined assuming 1 mol CH_3O formed per mol CH_4 reacted (Reaction conditions: 473 K, 2.9 kPa N₂O, 1.5 kPa CH_4 , 2 h, activated at 523 K in He for 12 h). No product formation detected in the presence of only 0.12 kPa H_2O .

H ₂ O Partial Pressure / kPa	CH ₃ OH Partial Pressure / kPa	$ m CH_4~Reacted \ / mol~(mol~M)^{-1}$	C_2H_4O Formed / mol (mol M) ⁻¹	$\begin{array}{c} mol \ C_2H_4O \ (mol \\ CH_3O)^{-1} \end{array}$
0.12	0	0.14	0.121	0
0.12	0.12	0.13		0.93

The role of water in acetaldehyde formation was investigated further by testing the reactivity of ethanol over activated MIL-100(Cr). Stoichiometric conversion of ethanol was observed at 373 K over activated MIL-100(Cr) in quantities consistent with the density of Cr^{2+} sites (Table 2 and Figure S15b). Lower activation temperatures that allow for the concurrent presence of Cr^{2+} and Cr^{3+} -OH⁻groups enable acetaldehyde formation in amounts that track with Cr^{2+} density, but activation under vacuum at 523 K which creates Cr^{2+} sites far in excess of terminal hydroxyls (Cr^{3+} -OH⁻) results in a decrease in cumulative acetaldehyde formation (Figure 9). Specifically, cumulative moles of acetaldehyde formed (0.07 mol (mol $Cr)^{-1}$) under this activation condition more closely approximate the moles of terminal hydroxides (0.05 mol Cr^{3+} -OH⁻ (mol $Cr)^{-1}$) than the moles of reduced metal sites (0.28 mol Cr^{2+} (mol $Cr)^{-1}$), suggesting that while methoxy formation is predicated on the availability of reduced metal sites, terminal hydroxides may be necessary for the dehydrogenation of ethanol to acetaldehyde.

Table 2. For MIL-100(Fe) and MIL-100(Cr), the activation condition employed, the corresponding M^{2+} site density, and the total quantity of acetaldehyde formed when ethanol (0.11 kPa) is fed over the activated material at 373 K.

Material	Activation Condition	M ²⁺ Site Density / mol (total mol M) ⁻¹	C_2H_4O Formed / mol (total mol M) ⁻¹
Cr	Inert flow, 523 K	0.16	0.13
Fe	Inert flow, 423 K	0.11	0.12



Figure 9. Cr^{2+} open-metal and Cr^{3+} -OH⁻ site densities (left axis) with increasing extent of activation and the corresponding quantity of acetaldehyde formed (right axis) when ethanol (0.11 kPa) is fed over MIL-100(Cr) at 373 K following thermal activation in He or vacuum (when indicated).

To further investigate the role of water in methane conversion to methanol/acetaldehyde, methoxy extraction was carried out over MIL-100(Cr) at varying water partial pressures while keeping the total water flow rate constant, and also at varying water flow rates while keeping the water partial pressure constant (Figure 10, Table S7). Regardless of water flow rates and partial pressures, water, methanol, and acetaldehyde break through simultaneously, consistent with methanol formation resulting from primary reactions between surface methoxies and water, and acetaldehyde resulting from secondary reactions between methoxies and gas phase methanol. The primary(/secondary) nature of methanol(/acetaldehyde) is consistent with the water breakthrough time- the time required for the edge of the water concentration front to reach the bottom of the MIL-100(Cr) bed- being identical to the time required for both methanol and acetaldehyde

to elute through the bed. The rank of products in these stoichiometric reactions is also consistent with the relative sharpness of their concentration fronts; methanol, which breaks through with water, exhibits significantly sharper concentration profiles compared to acetaldehyde (the secondary product), and elutes from the bed exclusively during the period when water molar flow rates at the exit of the bed lie between zero and that at the inlet. In fact, acetaldehyde fronts are broad enough that acetaldehyde is produced through methanol-methoxy interactions long after methanol ceases to be detected at the outlet of the bed (Figure 10).

Water partial pressures not only enable us to tune the relative number of primary (methoxy-water) interactions to secondary (methoxy-methanol) interactions as shown in Figure 10, but also the possibility of water-methoxy interactions in the first place. The stoichiometric nature of both these interactions suggests that under conditions where acetaldehyde is the exclusive product the ratio of moles of acetaldehyde formed to methoxies consumed should lie between 0.5 and 1, with a ratio of 0.5 indicating that every molecule of acetaldehyde owes its formation to an interaction between a methoxy species with a methanol molecule that is desorbed into the gas phase subsequent to a primary interaction with water (Scheme 2b). A ratio of unity, on the other hand, indicates the exclusive participation in methanol-methoxy interactions of methanol molecules fed at the *inlet* of the reactor, and the lack of C-C bond formation contributions from methanol molecules generated 'in-situ' through water-methoxy interactions (Scheme 2c).



Figure 10. Effect of water partial pressure (0.35 - 0.70 kPa) and flow rate $(1.54 - 3.07 \times 10^{-6} \text{ mol H}_2\text{O s}^{-1})$ on the CH₃OH and C₂H₄O selectivity over MIL-100(Cr) as indicated by the molar flow rates detected for both products at the reactor outlet as a function of time. (Extraction at 473 K, Reaction conditions: 473 K, 2.9 kPa N₂O, 1.5 kPa CH₄, 2 h, activated at 523 K in He for 12 h)

Scheme 2. (a) Representation of the MIL-100 surface following the reaction of CH_4 and N_2O in which 1 mol methoxy is formed per mol CH_4 reacted. (b) Formation of acetaldehyde exclusively through the secondary reaction of CH_3OH molecules formed 'in-situ' (blue) (c) Formation of acetaldehyde exclusively by reaction with CH_3OH fed at the inlet (black), resulting in the formation of 1 acetaldehyde molecule per methoxy

consumed.



This ratio captures the fraction of methoxies that interact with gas phase methanol of either kind to form acetaldehyde, with larger values indicative of greater relative contributions from methanol fed at the inlet versus those formed in-situ. As expected, acetaldehyde formation: methoxy consumption ratios of 0.5 were observed when the extraction was carried out at 373 K in the presence of 0.35 kPa water due to the absence of co-fed methanol (Table 3). Interestingly, these ratios were still found to lie in the vicinity of 0.5 when 0.35 kPa methanol was co-fed with 0.35 kPa water, suggesting that fed methanol contributes negligibly toward acetaldehyde formation, which instead results exclusively from C-C bond formation events involving methanol generated in-situ. A possible reason for the lack of participation of co-fed methanol may be the significantly slower movement of methanol through the MOF bed compared to water due to methanol outcompeting water from the standpoint of its affinity to open metal sites. Co-fed methanol is precluded from participating in secondary reactions due to the slower movement of its front through the MIL-100(Cr) bed, which results in fed methanol accessing only those regions of the bed that have been already been depleted of methoxies through interactions with the more rapidly progressing water concentration front. Such displacement of water by methanol is consistent with the rollover of water to flow rates exceeding those at the inlet (Figure 8b)- flow rates that likely accelerate the progress of methanol and acetaldehyde fronts generated in-situ. Reducing the water concentration to 0.12 kPa in the absence of co-fed methanol, on the other hand, reduces methanol and acetaldehyde formation rates to values below the detection limit of the mass spectrometer (Figure 8a). Introduction of equimolar water-methanol feeds at these pressures (0.12 kPa each) result in approximately the same number of moles of acetaldehyde formed as methoxies consumed, consistent with the lack of water methoxy interactions at these low water pressures (Table 1). The reaction of methoxies exclusively with methanol (but not water) at identical pressures of each reactant captures the propensity of MIL-100(Cr) to form C-C bonds, and the resulting prevalence of C-C bond formation steps at water pressures lower than those required for methoxy-water interactions. These interactions are significantly more challenging to deconvolute under conditions where C-C bond formation can also occur between methoxies and methanol molecules that result from water-methoxy interactions. The data presented in Table 3 suggest that exercising precise control over the relative preponderance of water-methoxy and methanol-methoxy interactions is highly non-trivial due to the fact that water-methoxy interactions can an increase local methanol concentrations that in turn make secondary reactions of methanol more probable, and may constitute part of the explanation as to why increasing water partial pressures appear to have an outsized effect on methanol-methoxy interactions compared to water-methoxy interactions (Figure 10).

Table 3. Comparison of the cumulative moles of CH_4 reacted and C_2H_4O formed over MIL-100(Cr) when the product extraction step is conducted under different partial pressures of H_2O and CH_3OH at 373 K. C_2H_4O to methoxy ratios are determined for 1 mol CH_3O formed per mol CH_4 reacted. (Reaction conditions: 473 K, 2.9 kPa N₂O, 1.5 kPa CH_4 , 2 h, activated at 523 K in He for 12 h).

H ₂ O Partial Pressure / kPa	CH ₃ OH Partial Pressure / kPa	$ m CH_4~Reacted~/mol~(mol~M)^{-1}$	C_2H_4O Formed / mol (mol M) ⁻¹	${ m mol} \ { m C_2H_4O} \ ({ m mol} \ { m CH_3O})^{-1}$
0.35	0	0.15	0.069	0.46
0.35	0.35	0.14	0.078	0.56

3.4. Prevalence of primary versus secondary reactions over tri-iron nodes

The ability of MIL-100(Fe) to convert methane to methanol has been reported by multiple groups. As described above, under identical conditions (0.35-0.70 kPa H₂O, 373-473 K), MIL-100(Cr) exhibits a propensity to convert methane to C2 oxygenates through secondary interactions of methanol with methoxy species formed on Cr^{2+} sites. C2 oxygenate formation, however, appears to not necessarily be precluded on MIL-100(Fe) materials, as demonstrated by the formation of ethanol upon product extraction with methanol at 0.12 kPa and 373 K (Figure 7b), and by the formation of acetaldehyde upon feeding ethanol over the partially-dehydrated material (0.11 kPa ethanol, 373 K - Figure S15a, Table 2). To test whether C2 oxygenate formation could occur over tri-iron clusters upon extraction with water, the water partial pressure during extraction was increased from 0.35 to 1.0 kPa (Figure 11), resulting in the detection of minor amounts of acetaldehyde (fractional molar selectivity = 0.03). Analogous to tri-chromium clusters, increasing inlet water partial pressures can be used to 'force' secondary reactions between Fe³⁺-methoxies and methanol, but the water partial pressures and/or flow rates required to access meaningful cumulative acetaldehyde selectivities may be much higher on tri-iron nodes than tri-chromium ones. Accessibility to C2 oxygenate production within lower water partial pressure and flow rate regimes enabled by MIL-100(Cr) likely reflect the greater propensity for Cr³⁺-OCH₃-intermediates to undergo C-C bond formation reactions with gas phase methanol compared to Fe^{3+} -OCH₃-intermediates, and point to metal identity being a reliable lever for tuning product selectivity in the partial oxidation of light alkanes over supported poly-metal oxo clusters.



Figure 11. Molar flow rates of CH₃OH, H₂O, and C₂H₄O at the reactor outlet as a function of time when (a) 0.35 kPa H₂O or (b) 1.0 kPa H₂O is fed over MIL-100(Fe) at 473 K following the oxidation of CH₄(reaction conditions: 473 K, 2.9 kPa N₂O, 1.5 kPa CH₄, 2 h, activated at 523 K in He for 12 h).

4. Conclusions

Tri-iron and tri-chromium nodes on MIL-100 frameworks effectuate the conversion of methane to methanol and acetaldehyde at low temperatures and sub-ambient reactant pressures. In-situ titrations with NO over MIL-100(Fe), combined with the equivalence between methoxy densities and Cr^{2+} open-metal site concentrations in MIL-100(Cr) across a range of thermal activation conditions suggest that the formation of both products occurs solely over M^{2+} sites. CO_2 transient formation rates that are insensitive to Fe^{3+} methoxy coverages, water titrations over surfaces pre-titrated with NO, and cumulative CO_2 yields per M^{3+} site that remain invariant as a function of activation temperature all point to the involvement of M^{3+} sites in deep oxidation. Methoxy intermediates play a key role in both methanol and acetaldehyde formation, with acetaldehyde formation in the absence of co-fed methanol occurring through secondary reactions of methanol molecules formed as a result of primary methoxy-water reactions. Acetaldehyde formation does not occur when purely methanol is fed over a methoxy-covered surface, suggesting that the presence of water is necessary for producing acetaldehyde, not ethanol, as the C2 oxygenate. Relative rates of propagation of water and methanol concentration fronts determine the ratio of cumulative methoxy-water and methoxymethanol encounters, and hence acetaldehyde selectivity; we show that these encounters can be 'forced' in either direction by varying inlet water partial pressures and/or flow rates. Although tri-chromium and tri-iron nodes both enable C-C bond formation steps, tri-chromium ones do so at significantly lower water extraction pressures, evidencing the potential for tuning C2 oxygenate selectivity merely by varying the identity of the metal atom constituting the oxo-bridged trimer. Elucidation of the role of metal identity and oxidation state in C-H bond scission and C-C bond formation steps is enabled, first and foremost, by the high level of definition, uniformity, and thermal stability of MIL-100 nodes. We assert, in this vein, that the study and use of MOF materials toward catalytic applications more generally could play a meaningful role in overcoming persistent limitations in the development of structure-property relationships that result at least in part directly from intractable levels of heterogeneity in (in)active site speciation.

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