# Peroxidative Halogenation Catalyzed by Transition-Metal-Ion-Grafted Mesoporous Silicate Materials

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The high density of surface silanol groups of mesoporous materials, which have large surface areas (1000−1600 m^2/g) and variable pore diameters (15−150 Å), provide attractive anchoring sites on which to graft organic moieties or transition metal ions[1,2] for chemical sensors and catalytic applications. Catalytic activities of transition-metal-associated mesoporous materials that have been investigated include hydroxylation of benzene, epoxidation of alkenes, and oxidation of di-*tert*-butylphenol, among others.[2−7] With the large surface areas and monodisperse pore sizes, these materials offer the possibility of creating reaction sites and molecular confinement that permit the selective formation of reaction products formed in biocatalytic processes.[8,9] Catalytic halogenation reactions are presently carried out with haloperoxidase enzymes. For instance, vanadium bromoperoxidase (V-BrPO) catalyzes the bromination of a variety of organic substrates (eq 1; RH is the organic substrate) under mild conditions using hydrogen peroxide as an oxidant of bromide.[10]

$$H_2O_2 + X^- + R-H + H^+ \rightarrow R-X + 2H_2O \qquad (1)$$
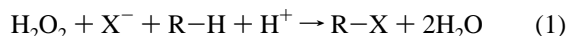
The oxidized bromine species can then brominate an organic substrate or oxidize a second equivalent of hydrogen peroxide, producing singlet oxygen.[11] Functional mimics of V-BrPO have been discovered recently (e.g., VO_2^+,[12] MoO_3(aq),[13] WO_3(aq),[13] Schiff-base complexes of V(V),[14,15] $MeReO_3$,[16] MoO(oxalato)[17]); however, unlike V-BrPO which functions optimally at

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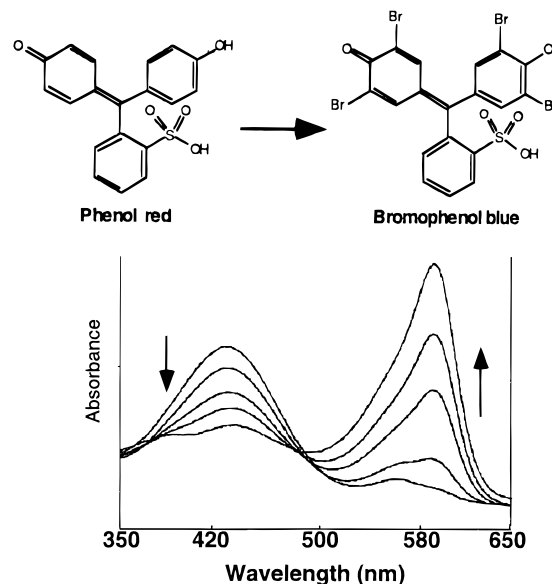
Figure 1. Peroxidative bromination of phenolsulfonephthalein (phenol red) catalyzed by Ti/MCM-48. Conditions: 3 mL of 0.2 mM phenol-sulfonephthalein sodium salt, 0.1 M KBr, 10 mM H_2O_2 in 0.1 M Hepes buffer, pH 6.5. The reaction was initiated by the addition of 7.2 mg of 5% Ti/MCM-48 and the samples were shaken at ∼250 rpm. The solution spectra were recorded at A, 10 min; B, 27 min; C, 60 min; D, 77 min; and E, 137 min. The spectra were obtained by removing the solid catalyst from the solution before running each UV−vis spectrum. The same qualitative results were obtained with Ti/MCM-48 prepared by the hydrothermal synthesis for the incorporation of titanium.

near neutral pH,[10] the vanadium biomimics require an acidic medium or an added proton source for catalysis. We report herein that, like V-BrPO, titanium(IV)-grafted mesoporous silicate materials (e.g., Ti/MCM-48[18] and Ti/MCM-41) efficiently catalyze peroxidative halogenation reactions in aqueous solution at neutral pH and in organic solvents. Ti/MCM-48 contains a three-dimensional bicontinuous cubic pore array[19−21] within the silicate structure onto which Ti(IV) has been grafted.[18] Ti/MCM-41 contains a one-dimensional hexagonal pore array onto which Ti(IV) has been grafted.[2]

When Ti/MCM-48 or Ti/MCM-41 (7−30 mg) is reacted with 10 mM hydrogen peroxide, 0.1 M potassium bromide, and 0.2 mM phenolsulfonephthalein (phenol red, λ_{max} 450 nm) in 0.1 M Hepes buffer pH 6.5 (3 mL total volume), 3′,3′′,5′,5′′-tetrabromophenolsulfonephthalein (tetrabromophenol blue, λ_{max} 589 nm[22]) is formed (Figure 1). Bromination does not occur with the pure MCM-48 or MCM-41 silicate materials, i.e., materials which lack incorporated Ti(IV) or other transition metal ions, establishing the catalytic requirement of bound Ti-(IV).[23] The UV−vis diffuse reflectance spectrum of Ti/MCM-

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(23) Quantitative conversion of phenol red to tetrabromophenol blue was also observed at a much higher concentration of phenol red, i.e., 5 mM (under conditions of 0.1 M KBr, 5 mg of 5% Ti/MCM-48 in 0.1 M Hepes buffer pH 6.5 with two aliquots of H_2O_2 (50 and 20 mM)). Bromination or bromoperoxidative oxidation of other substrates has also been carried out, including monochlorodimedone, the classic substrate used to measure haloperoxidase activity, 1,3,5-trimethoxybenzene, and various dyes (e.g., malachite green, murexide, fluorescein).
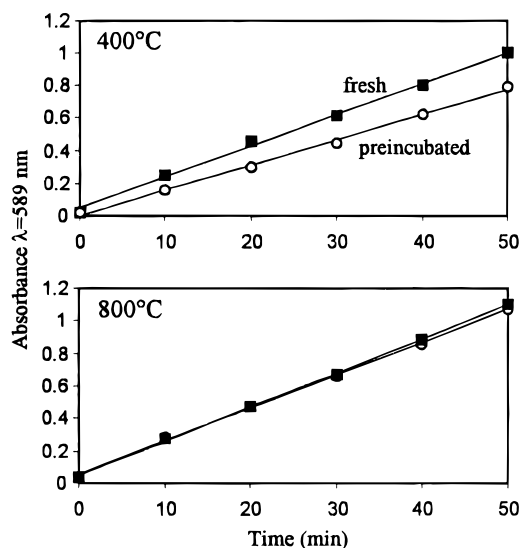
Figure 2. Comparison of the activity of 10% Ti/MCM-48 prepared by calcination at 400 and 800 °C. Activity was followed by peroxidative bromination of phenol red under conditions of 0.25 mM phenolsulfonephthalein sodium salt, 0.1 M KBr, 10 mM H_2O_2 in 0.1 M Hepes buffer, pH 6.5 (total volume 3 mL) with 10 mg of Ti/MCM-48 catalyst. The reactions were shaken at ~250 rpm. The preincubation was carried out in 1 mL of 0.1 M Hepes buffer, pH 6.5, for 39 h before its activity was measured. The Ti content in 10% Ti/MCM-48 was determined by elemental analysis.

48 upon addition of H_2O_2 shows an absorbance increase at *ca.* 400 nm relative to Ti/MCM-48, consistent with formation of peroxotitanium(IV) species (data not shown). This MCM-48-bound peroxotitanium(IV) species then oxidizes bromide reforming Ti/MCM-48. Thus, the function of Ti(IV) in Ti/MCM-48 is to coordinate and activate H_2O_2 for bromide oxidation. By contrast, the peroxo complex of TiO^{2+} in acidic aqueous solution, i.e., TiO_2^{2+}, stabilizes peroxide against oxidation of even iodide.[24]

The sole product of bromination of 2,3-dimethoxytoluene is ring-substituted bromo-2,3-dimethoxytoluene,[25] showing that the reaction is an electrophilic bromination process as opposed to a radical process for which 2,3-dimethoxybenzyl bromide would have been expected.[26] Thus, the two-electron oxidation of bromide by the silicate-anchored peroxotitanium(IV) moiety is consistent with formation of HOBr/OBr⁻ which would be in equilibrium with Br_2 and Br_3^-, depending on the pH and bromide concentration.

After extensive catalytic turnover or after incubation of 10% Ti/MCM-48 in buffer, the Ti/MCM-48 material that has been calcined at 400 °C loses activity (Figure 2, top). Ti/MCM-48 (10%) calcined at 800 °C, however, does not inactivate on incubation in aqueous solution (Figure 2, bottom). Thus, the high temperature calcination of Ti/MCM-48 leads to an exceptionally stable and reactive catalyst in aqueous solution, which is consistent with the removal of surface silanol defects and formation of additional SiO anchors to each Ti(IV) site during heat treatment. When the Ti content is increased to 18%, the same decrease in activity of preincubated *vs* fresh is also observed for material calcined at 400 °C (Figure 3, top) as that
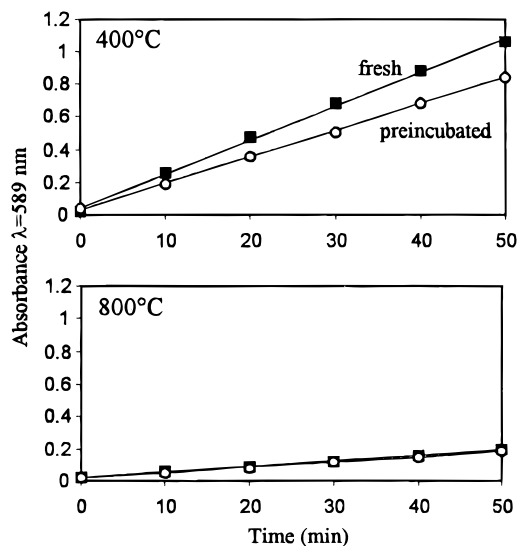

Figure 3. Comparison of the activity of 18% Ti/MCM-48 prepared by calcination at 400 and 800 °C. Same conditions as in Figure 2. The Ti content in 18% Ti/MCM was determined by elemental analysis.

for 10% Ti/MCM-48. However, the activity of 18% Ti/MCM-48 calcined at 800 °C drops significantly for both fresh and preincubated catalyst (Figure 3, bottom), although it is stable against inactivation in aqueous solution. The drop in activity is likely due to the formation of titania clusters, which is facilitated by the high Ti surface density, i.e., Ti/Si is 1:5.6 by elemental analysis. Once in a cluster, some of the titanium is not accessible for peroxide coordination and is thus inactive.

Ti/MCM-48 was active over a wide pH range (pH 4−8) and in a variety of organic solvents (e.g., ethyl acetate, tetrahydrofuran, acetonitrile, methanol) or aqueous−organic mixtures (e.g., 30% ethanol). In addition to Ti(IV), other transition-metal-grafted mesoporous materials were also found to catalyze peroxidative halogenation reactions, including V/MCM-48, Mo/MCM-48, and W/MCM-48.[18] Like the Ti/MCM materials, these catalysts work over a wide pH range and in organic solvents. Peroxidative chlorination of phenolsulfonephthalein was also observed in 0.1 M citrate buffer, pH 4 with 0.1 M KCl, but not at pH 6.5.

We have found that the Ti/MCM materials efficiently catalyze peroxidative halogenation reactions. As such, they are the first functional biomimics of vanadium bromoperoxidase which perform at neutral pH. The haloperoxidase reaction (eq 1) requires the consumption of an equivalent of H⁺ per turnover cycle. With Ti/MCM-48 or Ti/MCM-41 in buffered aqueous solution (pH 4−8) or an organic solvent, added acid is not required. IR experiments are in progress to identify the origin of the protons. We are also pursuing further investigations of the reactivity of the transition-metal-grafted MCM materials, including the selectivity of halogenation and oxidation reactions. Catalytic halogenation has many useful applications in synthetic organic chemistry, both as end products and as synthons. Thus, transition-metal-ion-grafted MCM materials offer a simple, useful, and direct approach to catalytic halogenation.

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