Bio-inspired oxidation of methane in water catalyzed by N-bridged diiron phthalocyanine complex†

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A stable μ-nitrido diiron phthalocyanine activates H_2O_2 to oxidize CH_4 in water at 25–60 °C to methanol, formaldehyde and formic acid as evidenced using ^{13}C and ^{18}O labelling.

A selective low temperature oxidation of methane is a long standing challenge.[1] In Nature, methane monooxygenase enzymes (MMO) transform CH_4 to CH_3OH in water under physiological conditions.[2–4] Considerable research has been dedicated to modelling of MMO. Complexes mimicking a structural organisation and spectral features of MMO have been described,[5,6] but *real functional chemical models capable of oxidizing CH_4 are still to be created.* Along with biomimetic studies, a low temperature oxidation of CH_4 has been inspired by the work of Shilov and co-workers on CH_4 activation on Pt.[7,8] Perspectives and challenges of C–H bond activation at metal centres have been reviewed.[9] Salts of Hg, Tl, Pd and Au promoted oxidation of CH_4 in oleum or H_2SO_4.[10] Stabilization of Pt or Pd by appropriate ligands and using oleum as the terminal oxidant allowed a catalytic process.[11] The CH_4 oxidation in oleum containing Pt(II) bipyrimidine complex at 220 °C provided the selective formation of methyl bisulfate.[11a] The combination of this complex with polyoxometallate allowed oxidation of CH_4 to CH_3OH and CH_3CHO with TON ~30.[12] Oxidative condensation of CH_4 to CH_3COOH in a $PdSO_4$–H_2SO_4 system at 180 °C provided TON of 5–18.[11b] Harsh conditions (strong concentrated acids, high temperature) are often applied to oxidize CH_4.

In contrast with organometallic CH_4 activation, MMO proceeds *via* a different mechanism, by creating a very strong oxidizing diiron species able to attack a C–H bond in CH_4. An essential feature of MMO is an active site containing two iron centres. However, for diiron synthetic models of MMO oxidation of CH_4 have yet to be achieved despite considerable efforts which were concentrated on non-heme complexes.[5] Notably, the use of binuclear porphyrin-like complexes for CH_4 oxidation has so far been completely neglected. Our studies on metallophthalocyanines (MPc) as catalysts for clean oxidation processes[13] showed that FePc supported in μ-oxo dimeric form (Fe–O–Fe fragment) exhibited better catalytic properties than monomer FePc.[13g] This finding prompted us to study binuclear MPc as oxidation catalysts.

μ-Nitrido iron phthalocyanine complex $(FePc)_2N$ contains two equivalent iron centres with a formal +3.5 oxidation state bridged *via* nitrogen (Fig. 1).[14] $(FePc)_2N$ is insoluble in organic solvents which makes its purification and use in catalysis difficult. To overcome this drawback we prepared iron μ-nitrido tetra-*tert*-butylphthalocyanine, $(FePc^tBu_4)_2N$.[15] Stable and inert μ-nitrido bridged iron complexes have never been evoked as oxidation catalysts although the first μ-nitrido iron porphyrin complex was described in 1976.[16]

We have observed that $(FePc^tBu_4)_2N$ interacts with biologically and ecologically relevant H_2O_2. The addition of H_2O_2 to a solution of $(FePc^tBu_4)_2N$ changed UV–Vis and EPR spectra.[15] $(FePc^tBu_4)_2N$ exhibited a signal at $g = 1.99$ indicative of one unpaired electron and a low spin Fe(III) state. After addition of H_2O_2 at 25 °C we detected a strong signal at $g = 4.25$ and a feature at $g = 8.16$ along with an enlarged signal at $g = 2.07$ and a small signal at $g = 1.99$ of the $(FePc^tBu_4)_2N$ left.[15] EPR parameters of new species are close to those of high and low spin Fe(III) peroxo complexes.[17] The diiron structure was kept intact as evidenced by positive electrospray ionization mass spectrometry (ESI-MS). ESI-MS spectra of $(FePc^tBu_4)_2N$ in MeCN containing H_2O_2 were remarkably clean.[15] Along with a signal at $m/z = 1599.8$ of the parent $(FePc^tBu_4)_2N$, a signal at $m/z = 1615.9$ corresponding to ^{16}O-$(FePc^tBu_4)_2N$ was detected. When $H_2{}^{18}O_2$ was used instead of $H_2{}^{16}O_2$ the spectrum had a signal at $m/z = 1617.9$ due to ^{18}O-$(FePc^tBu_4)_2N$ (Fig. 2). Isotopic patterns of the molecular peak obtained with $H_2{}^{16}O_2$ and $H_2{}^{18}O_2$ were identical to theoretical ones. When cyclohexene was added to the solution containing $(FePc^tBu_4)_2N$ and H_2O_2 the signal of O-$(FePc^tBu_4)_2N$ practically disappeared in favour of initial $(FePc^tBu_4)_2N$.[15] This result strongly suggests that oxygen originating from H_2O_2 is located at Fe, thus oxidizing cyclohexene, and not at a phthalocyanine moiety. No signal of monomer

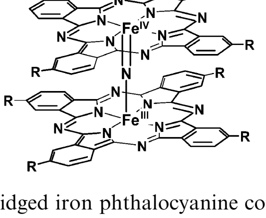

Fig. 1 μ-Nitrido-bridged iron phthalocyanine complexes. R = H or $C(CH_3)_3$ for μ-nitrido complex of iron phthalocyanine $(FePc)_2N$ and iron tetra-*tert*-butylphthalocyanine $(FePc^tBu_4)_2N$, respectively.

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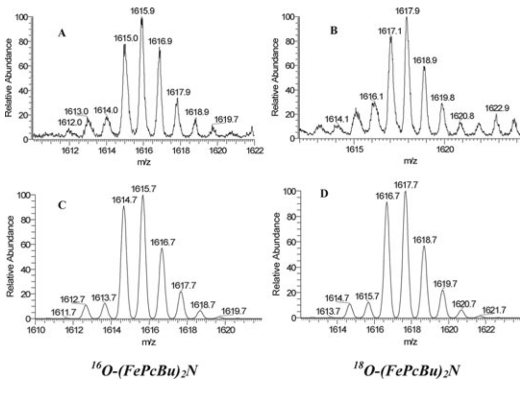

Fig. 2 ESI-MS spectra of oxo-$(FePc^tBu_4)_2N$ prepared in the reaction between $(FePc^tBu_4)_2N$ and $H_2{}^{16}O_2$ or $H_2{}^{18}O_2$ (MeCN, 25 °C): isotope distribution patterns of the molecular peak cluster for ^{16}O-$(FePc^tBu_4)_2N$ (A) and ^{18}O-$(FePc^tBu_4)_2N$ (B), and simulated isotope distribution patterns for these species (C and D, respectively).

$FePc^tBu_4$ was detected during ESI-MS experiments, indicating the stability of the Fe–N–Fe structure in the presence of H_2O_2.

The first catalytic tests showed very strong oxidizing properties of the $(FePc^tBu_4)_2N$–H_2O_2 system and prompted us to try the oxidation of CH_4. Initial tests with CH_4 were performed in MeCN containing 0.1 mM $(FePc^tBu_4)_2N$ and 67 mM H_2O_2. Formic acid was the main product along with traces of acetic acid, methanol, acetone and MeCN oxidation products.

To distinguish between the oxidation of CH_4 and the possible oxidation of CH_3CN, the reaction was performed in CD_3CN. GC–MS analysis of formic acid obtained in 6 mM concentration showed 68% of HCOOH and 32% of DCOOH, thus indicating parallel oxidation of CH_4 and CD_3CN in 2 : 1 ratio.[15] Kinetic analysis shows that this ratio is not compatible with a free radical mechanism of oxidation.[15] Reaction constants of $OH^\bullet$ with CH_4 and MeCN are 3.80×10^6 and $1.14 \times 10^7\ M^{-1}\ s^{-1}$, respectively. If $OH^\bullet$ were involved, the ratio *products derived from CH_4/products derived from MeCN* would be equal to $3.80 \times 10^6 \times 0.02\ M/1.14 \times 10^7 \times 19.17\ M = 1 : 2880$ where 0.02 and 19.17 M are the concentrations of CH_4 and MeCN, respectively. The catalytic oxidation of CH_4 occurred with a high turnover number of 40.8. However, the situation is complicated by the oxidation of the organic solvent which is difficult to avoid in the presence of active species strong enough to oxidize CH_4.

The best solution to avoid uncertainties due to solvent oxidation is to use water, an inert, green and biologically relevant solvent. With this aim, μ-nitrido complex was supported onto silica.[15] Heterogeneous oxidations of CH_4 were performed in pure H_2O. The CH_4 oxidation was unambiguously evidenced using labelled $^{13}CH_4$ in D_2O at 60 °C. When the mixture of 53% of CH_4 and 47% of $^{13}CH_4$ was used for oxidation, the ^{13}C NMR spectrum of the final reaction mixture showed two signals at 81.6 and 165.5 ppm attributed to hydrated formaldehyde $^{13}CH_2(OH)_2$ and $H^{13}COOH$, respectively.† Neither $^{13}CH_3OH$ (49 ppm) nor $^{13}CO_2$ (125 ppm) signals were found in this spectrum. CH_2O and HCOOH were therefore the main products of CH_4 oxidation. GC–MS analysis of the reaction using the same $CH_4/^{13}CH_4$ ratio (53/47) run in H_2O (to avoid an artefact due to possible H/D exchange in HCOOH with D_2O) indicated 56% of HCOOH and 44% of $H^{13}COOH$ corresponding to the isotopic composition of CH_4.[15] Methanol was also detected and contained $^{13}CH_3OH$ and CH_3OH in 1 : 1 ratio. Acetic acid and acetone didn't contain ^{13}C label, suggesting that they were not derived from CH_4 and were probably formed from the oxidation of the catalyst. The stability of CH_3OH under the reaction conditions was tested using 0.01 M CH_3OH solution in water. The conversion of CH_3OH was 82% after 1 h and the HCOOH yield was 80%. CH_3OH is the primary product of oxidation which is converted to CH_2O and HCOOH under reaction conditions (Fig. 3).

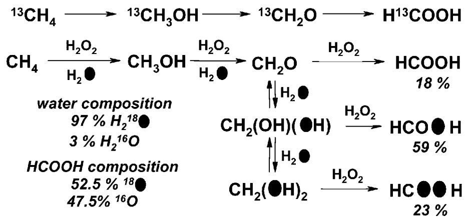

Fig. 3 Oxidation of methane using ^{13}C and ^{18}O labelling.

When the reaction was performed in 97% $H_2{}^{18}O$, CH_3OH didn't contain ^{18}O, indicating that its oxygen originated from $H_2{}^{16}O_2$.[15] Formic acid was composed of 18% of $HC^{16}O_2H$, 59% of $HC^{16}O^{18}OH$ and 23% of $HC^{18}O_2H$. The exchange of intermediate hydrated formaldehyde and formic acid with $H_2{}^{18}O$ could result in introduction of ^{18}O in HCOOH (Fig. 3).

The oxidation of CH_4 was tested at different temperatures. Remarkably, the oxidation of CH_4 was still efficient even at 25 °C, providing HCOOH with TON = 13 (Table 1, run 1). At 40–50 °C HCOOH and CH_2O were obtained in ~2 : 1 ratio (runs 2 and 3). At higher temperature the amount of CH_2O diminished in favour of HCOOH. The activity of the catalyst was similar between 40 and 80 °C, providing 26–32 turnovers.

Based on the results obtained by UV–Vis, EPR, ESI-MS techniques and in labelling experiments, we propose a tentative mechanism of the oxidation of CH_4 (Fig. 4). In the first step, $(FePc^tBu_4)_2N$ coordinates H_2O_2 to form hydroperoxo complex $Fe^{IV}NFe^{III}OOH$ which is probably in equilibrium with the deprotonated form $Fe^{IV}NFe^{III}OO^-$. $(FePc^tBu_4)_2N$ oxo complex could be formed from $Fe^{IV}NFe^{III}OOH$ *via* heterolytic cleavage of the O–O bond. Recent DFT calculations showed that water favoured the formation of non-heme HO–$Fe^V{=}O$ species *via* water-assisted O–OH bond cleavage.[18] Recently, chemical and spectroscopic evidence for an Fe^V–oxo complex was obtained.[19] Otherwise, a homolytic cleavage of the O–O bond in $Fe^{IV}NFe^{III}OOH$ would form $Fe^{IV}NFe^{IV}{=}O$ with formation of OH radical. However, this pathway is not compatible with a high stability of the $(FePc^tBu_4)_2N$ core in the presence of H_2O_2 and with observed rates of CH_4 *vs.* MeCN oxidation. If $OH^\bullet$ were to be formed, $(FePc^tBu_4)_2N$ should be rapidly destroyed. High concentrations of HCOOH obtained in CH_4 oxidations and the relative reactivity of CH_4 and MeCN found in homogeneous conditions are also not compatible with free radical chemistry.[15]

The heterolytic cleavage of the O–O bond in $Fe^{IV}NFe^{III}OOH$ complex and the formation of putative very strong oxidizing $Fe^{IV}NFe^V{=}O$ species should be favoured in the presence of acid by the protonation of peroxide oxygen. Indeed, a significant

Table 1 Oxidation of methane by H_2O_2 in water catalyzed by supported $(FePc^tBu_4)_2N$ complex[a]

Run	T/°C	[HCOOH]/ mM	TON_{HCOOH}	[CH_2O]/ mM	TON_{CH_2O}	Total TON[b]
1	25	6.0	13.0	0	0	39.0
2	40	8.6	18.6	4.8	10.4	76.6
3	50	9.2	21.0	4.7	10.7	84.4
4	60	10.5	22.8	1.5	3.2	74.8
5	70	11.7	25.2	0.8	1.7	79.0
6	80	12.8	27.3	0.5	1.1	84.1
7[c]	60	69.0 (34.1)	134.6 (72.8)	7.6	16.5	436.8

[a] Conditions: 32 bars CH_4; 2 mL H_2O; catalyst, 0.925 μmol (0.875 μmol for run 3); 678 μmol H_2O_2; reaction time 20 h (48 h for run1). [b] Total TON was calculated as 3 × HCOOH/catalyst + 2 × $CH_2(OH)_2$/catalyst. [c] In 0.1 M H_2SO_4; 678 μmol H_2O_2 were added at reaction times 0 and 16 h. Values in parentheses were measured before the second addition of H_2O_2.

improvement of the catalytic activity was observed in the presence of 0.1 M H_2SO_4. The TON_{HCOOH} was increased by more than a factor of 3 to attain 72.8. After completion of the first reaction, a new portion of H_2O_2 was added directly to the reaction mixture. Remarkably, the catalytic system retained practically the same catalytic activity in the second cycle (Table 1, run 7), indicating a high stability of the catalyst and even a possibility of recycling. The catalyst exhibits a very high performance: more than 150 moles CH_4 per mole of catalyst were oxidized to useful products. This activity is far higher than that of most published systems operating *via* CH_4 activation[7–10,11b,12] and approaches that of the most efficient so far, Periana's system based on Pt(II) bipyrimidine complex in oleum at 220 °C.[11a] Total TON = 437 and 30–50% product yields on H_2O_2 were attained using $(FePc^tBu_4)_2N$. This catalytic system shows several attractive features: the clean oxidant (H_2O_2) and reaction medium (H_2O), and the fact that solid catalyst can easily be separated by filtration. In contrast to the much more expensive porphyrin and non-heme complexes, phthalocyanines can be accessible in bulk quantities.[20]

It should be noted that the Fe–N–Fe unit of $(FePc^tBu_4)_2N$ is essential for the catalytic activity. Terminal nitrido ligand stabilizes Fe^V and even Fe^{VI} states in mononuclear cyclam complexes.[21] One can suggest that μ-nitrido ligand in a diiron complex could also stabilize ultra high valent Fe states. Mononuclear $FePc^tBu_4$ and its diiron μ-oxo (Fe–O–Fe) and μ-carbido (Fe=C=Fe) complexes[15] showed no oxidation of CH_4. μ-Nitrido diiron complex and soluble MMO share a similar structural feature, binuclear iron sites. However, the coordination spheres of these sites are different. In MMO, the diiron centre contains four glutamate (carboxyl ligand) and two histidine (N-ligand) residues and two iron ions are connected *via* the carboxylate of glutamate and water or hydroxide fragments. Iron ions in μ-nitrido dimer are coordinated with four nitrogen atoms of planar exogenous phthalocyanine ligands which are nevertheless structurally related to endogenous porphyrin. Further research is necessary to provide deeper insights into this novel fascinating chemistry.

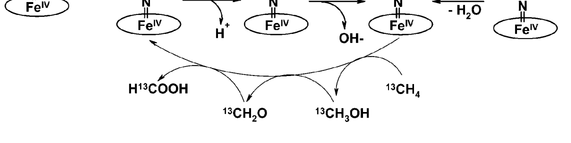

Fig. 4 Proposed mechanism of the formation of active species in the system $(FePc^tBu_4)_2N$–H_2O_2 and oxidation of methane. Fe^{IV}–N–Fe^V=O stands for species having 2 redox equivalents above the $Fe^{III}Fe^{IV}$ state.

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