

Microwave-Assisted Fast Cyclohexane Oxygenation Catalyzed by Iron-Substituted Polyoxotungstates

Marcella Bonchio,^{a,*} Mauro Carraro,^a Gianfranco Scorrano,^a Ulrich Kortz^b

^a Istituto CNR per la Tecnologia delle Membrane (ITM-CNR), Università di Padova, via Marzolo 1, 35131 Padova, Italy
Fax: (+39)-(0)49-827-5239, e-mail: marcella.bonchio@unipd.it

^b School of Engineering and Science, International University Bremen, P. O. Box 750 561, 28725 Bremen, Germany
E-mail: u.kortz@iu-bremen.de

Received: March 14, 2005; Accepted: August 31, 2005

Abstract: Under microwave irradiation, iron-substituted polyoxotungstates (Fe-POMs) catalyze cyclohexane oxygenation to A/K oil with 90–95% selectivity, unmatched turnover frequencies (40–400 h⁻¹), and multi-turnover regime (>1000 TON). Such a rapid reaction protocol allowed the screening of so-called inorganic Fe-synzymes with 1–4 nuclearity, including a family of Krebs-type isostructural complexes. Product distribution, kinetic analysis, mechanistic probes and fitting calculations, are consistent with a radical chain oxidation propagated by Fe-catalysed decomposition of organic peroxides which ultimately depends on the redox-properties and structural arrangement of the iron moiety within the POM cage.

Keywords: Aerobic oxidation; C–H bond activation; homogeneous catalysis; iron; microwave irradiation; polyoxometalates

The selective oxidation of cyclohexane to a mixture of cyclohexanol and cyclohexanone (K/A oil) is of considerable importance in the production of adipic acid (AA) finally used in the manufacture of polyamide fibers (nylon 6,6). The current industrial process employs homogeneous cobalt salts, molecular oxygen at 8–9 atm and temperatures above 150–160 °C to obtain cyclohexane conversions in the range 3–6% and a K/A oil selectivity

around 80%.^[1] A formidable challenge in both industrial and academic research is the invention of new catalysts performing efficiently with 1 atm O₂. In this direction, benchmark literature results can be ranked on the basis of the total turnover number (TON) and the turnover frequency (TOF) exhibited (Table 1). Inspection of these data shows a promising perspective for catalytic oxygenation with transition metal-substituted polyoxometalates (TMS-POMs). Indeed, polyoxometalates provide an inorganic coordination framework where a redox-active metal center (Fe, Mn, Ru, or others) is bound by MO₆ octahedra with M being generally Mo(VI), W(VI).

Noteworthy, some Fe-POMs display structural analogy to the active site of natural oxygenation enzymes (Figure 1).^[7] The synzyme rationale has been recently invoked to address the superior performance of γ-[(FeOH₂)₂SiW₁₀O₃₈]⁶⁻ in hydrocarbon oxygenation compared to homologues [(FeOH₂)_xSiW_(12-x)O_(40-x)]^{(4+x)-} where x = 1–3.^[3,8] However, the severe mechanistic complexity associated with metal-mediated aerobic oxidations hampers the understanding of the catalyst role and fate so that, in most cases, a claimed adherence to bioinspired guidelines remains doubtful.

Herein, we report on the screening of selected Fe^{III}-POM catalysts for cyclohexane oxygenation by a rapid reaction protocol under microwave (MW) induced dielectric heating. Such a novel approach takes advantage of the extreme robustness and polyanionic nature of the catalyst^[9] to elicit MW absorption.^[10] Our results include: (i) the discovery of hits operating at unprecedented peak ef-

Table 1. Benchmark systems for aerobic oxidation of cyclohexane with 1 atm O₂.

Catalyst	Conv. [%] (Time [h])	TON (TOF [h ⁻¹])	Ref.
γ-[(MnOH ₂) ₂ SiW ₁₀ O ₃₈] ⁶⁻	6.4 (96)	789 (8.2)	[2]
γ-[(FeOH ₂) ₂ SiW ₁₀ O ₃₈] ⁶⁻	1.1 (96)	135 (1.4)	[3]
Mn(acac) ₂ /NHPI	65 (20)	130 (6.5)	[4]
Fe(II)-picolinic acid	36 (9)	121 (13)	[5]
Co(acac) ₂ /NHPI	45 (6)	90 (15)	[6]

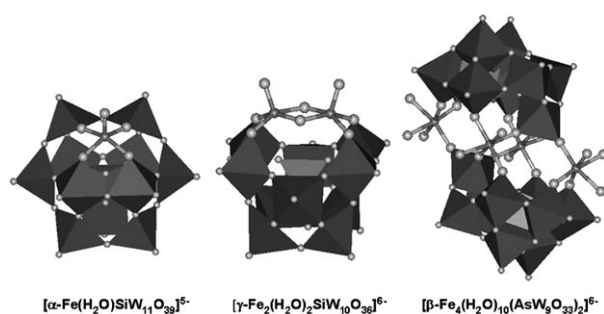


Figure 1. Structure of representative iron-substituted polyoxotungstates.

efficiency with TOF in the range 40–400 h^{−1} and total turnover number > 1000, (ii) examination of Fe^{III}-POMs, including a series of Krebs-type isostructural complexes, and (iii) the drawing of a general reaction scheme, based on mechanistic probes and fitting the oxidation kinetics.

Fe^{III}-POMs of nuclearities 1–4 were obtained by metalation of lacunary polyoxotungstates, yielding [α-Fe(H₂O)SiW₁₁O₃₉]^{5−} (FeSiW₁₁), [γ-Fe₂(H₂O)₂SiW₁₀O₃₈]^{6−} (Fe₂SiW₁₀), [α-Fe₃(H₂O)₃SiW₉O₃₇]^{7−} (Fe₃SiW₉) and [β-Fe₄(H₂O)₁₀(XW₉O₃₃)₂]^{n−} (Fe₄X₂W₁₈ with X = Se^{IV}, Te^{IV}, As^{III}, Sb^{III}, and n = 4, 6).^[11–14] These complexes were used as tetrahexylammonium (THA) salts in 1,2-dichloroethane (DCE). Data in Table 2 are meant to verify the catalyst activity and selectivity after 150–250 min MW irradiation. Cyclohexyl hydroperoxide (CHHP), cyclohexanol (A) and cyclohexanone (K) account for 90–95% selectivity.^[15]

Control experiments indicate that in the absence of catalyst or MW exposure, the oxidation is negligible or extremely slow (entries 1–3). Under MW irradiation,

FeSiW₁₁ performs with unmatched TOFs (entries 4–6).^[16] Moreover FT-IR spectra confirm that the recovered catalyst preserves the original structure, at variance with the organic porphyrin analogue (entry 7).^[17] In the case under study, converging lines of evidence delineate a radical chain mechanism, namely: (i) steady accumulation of the autooxidation product CHHP on lowering the catalyst loading (entries 4–6); (ii) acceleration by *tert*-butyl hydroperoxide (TBHP) (entry 8), (iii) inhibition by the radical scavenger 3,5-di-*tert*-butyl-4-hydroxytoluene (BHT) (entry 9), (iv) a biphasic kinetic trace, with a slow initiation phase followed by a fast zero-order regime, indicating an autocatalytic behavior (Figure 2).^[18]

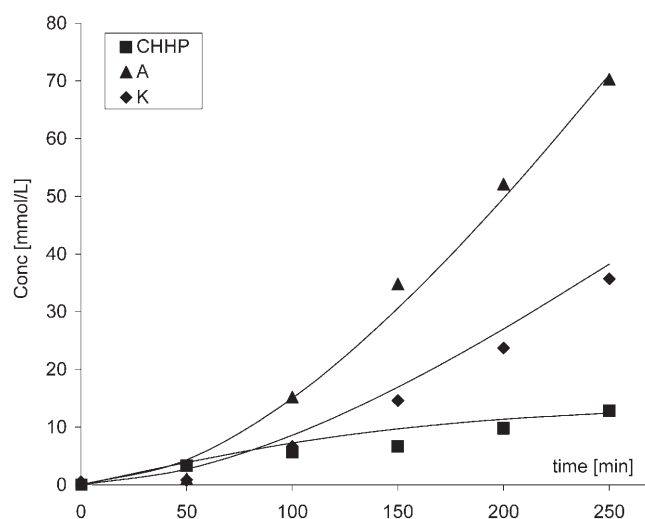


Figure 2. Experimental (points) and calculated (see Scheme 1) curves for run 6 in Table 1.

Table 2. Cyclohexane oxygenation by mononuclear Fe^{III} catalysts.^[a]

Entry	Catalyst [μmol]	Additive [μmol]	Time [min]	Conv. ^[b] [%]	Selectivity ^[c] CHHP:A:K	TON ^[d]	TOF ^[e] [h ^{−1}]
1	—	—	250	0.15	59:39:2	—	—
2	FeSiW ₁₁ (0.75) ^[f]	—	150	0.07	n.d.	n.d.	n.d.
3	FeSiW ₁₁ (0.75) ^[g]	—	5520	1.89	0:60:40	229	4.7
4	FeSiW ₁₁ (0.75)	—	250	2.95	0:66:34	358	141
5	FeSiW ₁₁ (0.38)	—	250	2.74	5:57:38	656	207
6	FeSiW ₁₁ (0.19)	—	250	2.42	11:60:29	1159	439
7	FeTMP (0.75) ^[h]	—	150	1.38	2:66:32	167	72
8	FeSiW ₁₁ (0.75)	TBHP (20)	150	2.40	5:64:31	291	147
9	FeSiW ₁₁ (0.75)	BHT (300)	150	<0.02	n.d.	n.d.	n.d.

^[a] DCE 0.8 ml, cyclohexane 9.1 mmol, O₂ 1 atm, T = 120 °C, applied power of MW irradiation = 240 W. FeTMP = iron (III) tetrakis(5,10,15,20-mesityl)porphyrin.

^[b] % of substrate conversion.

^[c] Product distribution.

^[d] Total turnover number (TON): products (mmol)/catalyst (mmol).

^[e] Highest turnover frequency calculated as TON per hour on the linear kinetic phase.

^[f] Conventionally heated at 120 °C.

^[g] Conventionally heated at 83 °C.

^[h] 90% catalyst decomposition determined by UV-Vis analysis at 418 nm.

Table 3. Cyclohexane oxygenation by Fe^{III}-POM catalysts.^[a]

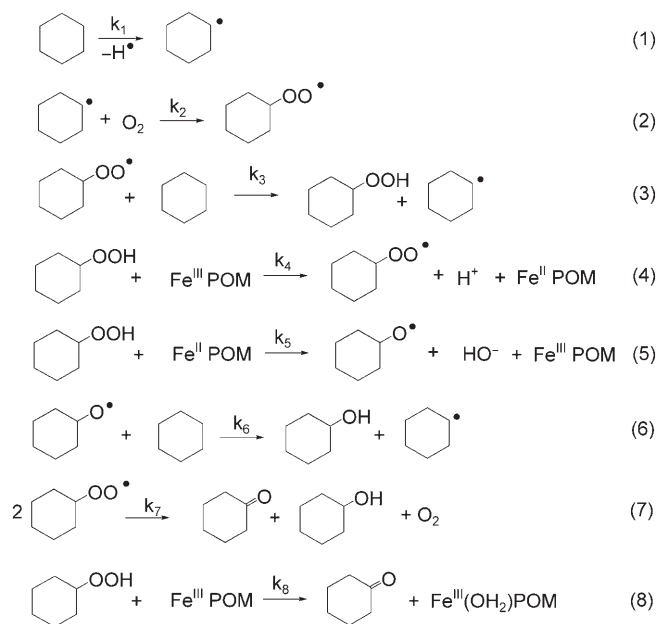
#	Catalyst ^[a]	Conv. ^[b] [%]	Selectivity ^[c] CHHP:A:K	TON ^[d]	TOF ^[e] [h ⁻¹]
1	FeSiW ₁₁	1.42	6:67:28	172	141
2	Fe ₂ SiW ₁₀	0.54	73:7:20	66	30
3	Fe ₃ SiW ₉	0.37	76:6:18	45	38
4	Fe ₄ Se ₂ W ₁₈	0.30	88:0:12	36	23
5	Fe ₄ Te ₂ W ₁₈	0.51	66:25:9	62	34
6	Fe ₄ Sb ₂ W ₁₈	0.57	45:35:20	69	37
7	Fe ₄ As ₂ W ₁₈	0.96	49:33:18	116	70

^[a] DCE 0.8 mL, cyclohexane 9.1 mmol, catalyst 0.75 μ mol, O₂ 1 atm, T = 120 °C, MW power 240 W for 150 min.

^[b–e] See footnotes in Table 2.

Therefore, the overall mechanistic hypothesis includes steps 1–8, (Scheme 1).^[19] In particular, because the TBHP-induced acceleration results from suppressing the initial lag-time while not affecting the propagation rate^[20] (*cf.* TOFs in entries 4 and 8), the main role of the iron catalyst may be envisaged in the propagation chain, promoting an efficient decomposition of CHHP through Haber–Weiss reductive and oxidative steps (Scheme 1, steps 4 and 5).^[20–22] Further support to such a scenario comes from the 2:1 A/K selectivity, which cannot be simply explained by the uncatalyzed Russell-type decomposition of the organic peroxide accounting for a selectivity ratio close to 1 (Scheme 1, step 7).^[21,23] This model turns out to fit the experimental kinetics (Figure 2) and identifies the relevant catalytic steps (4, 5 in Scheme 1) mainly within the propagation chain.^[24] The iron-mediated mechanism is also probed by the selectivity of adamantane oxidation, yielding a C-3/C-2 ratio of 9.5.^[25,26] this value falls within the expected range for a radical reaction (1–25) and is similar to those exhibited by analogous porphyrin catalysts (6–10).^[27] Although it is obviously problematic to encode such a multi-step mechanism by TON and TOF macro-parameters, which strongly depend on the catalyst loading (entries 4–6 in Table 2), they provide straightforward guidelines for process optimization.

A different behavior can be traced for substituted POMs with higher iron nuclearity, leading to CHHP accumulation and to increase of ketone (entry 1 *vs.* entries 2–7 in Table 3). Both features indicate a depressed peroxide decomposition *via* homolytic pathways, favoring heterolytic ketonization (Scheme 1, step 8).^[18,28] This latter reaction is known to proceed through a peroxometal intermediate whose nature and stability may depend on the structural arrangement of the iron moiety and on the POM tungsten framework.^[29] Nevertheless, along the series of the Krebs-type isostructural complexes, the overall oxidation efficiency can be ascribed to the redox properties of the iron moiety.^[14] In particular, the higher TOF process is given by Fe₄As₂W₁₈ which, together with the isocharged Fe₄Sb₂W₁₈ species, displays a well behaved cathodic wave at a higher reduction potential, thus suggesting that the catalyst is also participating in the Haber–Weiss chemistry.^[14] Studies are in



Scheme 1. Kinetic model of cyclohexane oxygenation catalyzed by Fe(III)-POMs.

progress to look at the interaction between Fe^{III}-POMs with model organic peroxides in order to gain insight into the nature of postulated peroxo-iron intermediates and their evolution to products through homolytic or heterolytic pathways. Our final aim is to obtain structure-activity correlations so to implement the design of new selective catalytic systems and exploit the rich and versatile chemistry of polyoxometalates.

Experimental Section

The iron substituted polyoxotungstates were prepared following literature procedures.^[11–14] THA salts were obtained by cation exchange in water.

General Oxidation Procedure

DCE (0.8 mL), Fe-POM (0.75–0.19 μ mol) and cyclohexane (0.98 mL) were mixed, under a dioxygen atmosphere, in a 10-

mL closed teflon reactor (HPR-1000/10S, Milestone) equipped with temperature and pressure control units and irradiated inside the cavity of a MW Ethos-1600 labstation (Milestone) at 240 W, with $T_{\text{bulk}} = 120^\circ\text{C}$ and $P_{\text{bulk}} \cong 2$ atm. In the system under examination, higher irradiation powers caused heating and pressure peaks which are detrimental for obtaining a reproducible heating profile. The reaction was sampled (50 μL) every 50 minutes always restoring the dioxygen atmosphere. The samples were analyzed by GLC and GLC-MS. Peroxide content was determined using the triphenylphosphine quencher method,^[30] carboxylic acids were revealed by silylation with BSTFA before GLC-MS analysis. Fe-POM stabilities were assessed by FT-IR after precipitation from the reaction mixture and washing with diethyl ether. Kinetic parameters were obtained by non-linear experimental data fitting with the *Scientist Micromath* software.

Acknowledgements

Financial support from the Italian National Council of Research is gratefully acknowledged.

References and Notes

- [1] K. Weissmermel, H. J. Arpe, *Industrial Organic Chemistry*, 2nd edn., VCH, Weinheim, **1993**.
- [2] T. Hayashi, A. Kishida, N. Mizuno, *Chem. Commun.* **2000**, 381–382.
- [3] C. Nozaki, M. Misono, N. Mizuno, *Chem. Lett.* **1998**, 1263–1264.
- [4] T. Iwahama, K. Syojyo, S. Sakaguchi, Y. Ishii, *Org. Process Res. Dev.* **1998**, 2, 255–260.
- [5] D. H. R. Barton, T. Li, J. MacKinnon, *Chem. Commun.* **1997**, 557–558.
- [6] Y. Ishii, T. Iwahama, S. Sakaguchi, K. Nakayama, Y. Nishiyama, *J. Org. Chem.* **1996**, 61, 4520–4526.
- [7] a) B. J. Wallar, J. D. Lipscomb, *Chem. Rev.* **1996**, 96, 2625–2658; b) M. Costas, M. P. Mehn, M. P. Jensen, L. Que Jr., *Chem. Rev.* **2004**, 104, 939–986; c) T. J. McMurry, J. T. Groves, in: *Metalloporphyrin Models for Cytochrome P-450*, (Ed.: P. R. Ortiz de Montellano), Plenum Press, New York, **1986**, pp. 1–28.
- [8] a) Y. Nishiyama, Y. Nakagawa, N. Mizuno, *Angew. Chem.* **2001**, 113, 3751–3753; *Angew. Chem. Int. Ed.* **2001**, 40, 3639–3641; b) N. Mizuno, C. Nozaki, T. Hirose, M. Tateishi, M. Iwamoto, *J. Mol. Catal. A: Chem.* **1997**, 117, 159–168; c) N. Mizuno, M. Hashimoto, Y. Sumida, Y. Nakagawa, K. Kamata, in: *Polyoxometalate Chemistry for Nano-Composite Design*, Kluwer Academic/Plenum, New York, pp. 197–203, **2002**; d) N. Mizuno, *Catal. Surv. Japan* **2000**, 4, 149–154.
- [9] C. L. Hill, C. M. Prosser-McCartha, *Coord. Chem. Rev.* **1995**, 43, 407–455.
- [10] M. Larhed, C. Moberg, A. Hallberg, *Acc. Chem. Res.* **2002**, 35, 717–727; b) A. Loupy *CR Chimie* **2004**, 7, 103–112; c) A. de la Hoz, A. Diaz-Ortiz, A. Moreno, *Chem. Soc. Rev.* **2005**, 34, 164–178.
- [11] F. Zonnevillle, C. M. Tourné, G. F. Tourné, *Inorg. Chem.* **1982**, 21, 2751–2757.
- [12] C. Nozaki, I. Kiyoto, Y. Minai, M. Misono, N. Mizuno, *Inorg. Chem.* **1999**, 38, 5724–5729.
- [13] J. Liu, F. Ortéga, P. Sethuraman, D. E. Katsoulis, C. E. Costello, M. T. Pope, *J. Chem. Soc. Dalton Trans.* **1992**, 1901–1906.
- [14] U. Kortz, M. G. Savelieff, B. S. Bassil, B. Keita, L. Nadjo, *Inorg. Chem.* **2002**, 41, 783–789.
- [15] Carboxylic acids were mainly observed as overoxidation products while significant chlorinated products were detected only under conventional heating likely originating from autoxidation pathways involving the solvent.
- [16] CH_3CN completely inhibits catalysis, thus explaining a previously reported observation.^[8]
- [17] Fe-TMP-catalyzed oxidation occurs with no induction time likely due to formation of organic radicals from ligand degradation.
- [18] R. A. Sheldon, J. K. Kochi, *Metal-Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, **1981**.
- [19] R. Pohorecki, J. Baldyga, W. Moniuk, W. Podgórska, A. Zdrójkowski, P. T. Wierzchowski, *Chem. Eng. Sci.* **2001**, 56, 1285–1291, and references cited therein.
- [20] a) M. Bonchio, V. Conte, F. Di Furia, G. Modena, *J. Org. Chem.* **1989**, 54, 4368–4371; b) M. Bonchio, V. Conte, F. Di Furia, G. Modena, S. Moro, J. O. Edwards, *Inorg. Chem.* **1994**, 33, 1631–1637.
- [21] A. S. Goldstein, R. S. Drago, *Inorg. Chem.* **1991**, 30, 4506–4510.
- [22] MW-induced super-heating is likely to promote the uncatalyzed initiation of the autoxidation.
- [23] G. A. Russel, *J. Am. Chem. Soc.* **1957**, 79, 3871–3877.
- [24] Calculated kinetic constants $k_1 = 7.0 \times 10^{-8} \text{ (s}^{-1}\text{)}$; $k_2 = 10^8 \text{ (s}^{-1}\text{)}$; $k_3 = 3.8 \text{ (L mol}^{-1} \text{ s}^{-1}\text{)}$; $k_4 \times [\text{Fe}^{\text{III}}] = 10^{-8} \text{ (s}^{-1}\text{)}$; $k_5 \times [\text{Fe}^{\text{II}}] = 2.8 \times 10^{-4} \text{ (s}^{-1}\text{)}$; $k_6 = 10^7 \text{ (L mol}^{-1} \text{ s}^{-1}\text{)}$; $k_7 = 10^8 \text{ (L mol}^{-1} \text{ s}^{-1}\text{)}$; $k_8 \times [\text{Fe}^{\text{III}}] = 0$.
- [25] The selectivity parameter is defined as the relative reactivity of tertiary to secondary CH groups calculated per H atom. Under the conditions explored (see footnotes in Table 1), adamantane (0.15 mmol) is oxidized, in chlorobenzene, to 1-adamantanol, 2-adamantanol and adamantanone in a relative ratio 76:16:8.
- [26] M. Bonchio, G. Scorrano, P. Toniolo, V. Artero, A. Proust, V. Conte, *Adv. Synth. Catal.* **2002**, 344, 841–844, and references cited therein.
- [27] a) Y. Ishii, S. Sakaguchi, T. Iwahama, *Adv. Synth. Catal.* **2001**, 343, 393–427; b) F. Minisci, F. Fontana, S. Araneo, F. Recupero, S. Banfi, S. Quici, *J. Am. Chem. Soc.* **1995**, 117, 226–232.
- [28] J. D. Chen, J. Dakka, R. A. Sheldon, *Appl. Catal. A: Gen.* **1994**, 108, L1–L6.
- [29] J. Kim, R. G. Harrison, C. Kim, L. Que Jr., *J. Am. Chem. Soc.* **1996**, 118, 4373–4379.
- [30] G. B. Shul'pin, *CR Chimie* **2003**, 6, 163–178.