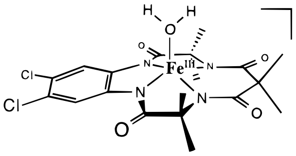
Ligand Design Approach for Securing Robust Oxidation Catalysts

Colin P. Horwitz, David R. Fooksman, Leonard D. Vuocolo,
Scott W. Gordon-Wylie, Nathaniel J. Cox, and
Terrence J. Collins*

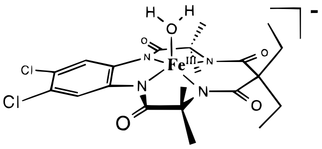
Department of Chemistry, Carnegie Mellon University
4400 Fifth Avenue, Pittsburgh, Pennsylvania 15213

Received August 18, 1997

Useful long-lived homogeneous oxidation catalysts based on metal complexes remain scarce in large part because oxidatively robust ligands are rare.[1] Noteworthy oxidation-resistant ligands include halogenated porphyrins,[2,3] some phthalocyanines,[4] and certain TACNs.[5] We have been developing oxidatively robust tetraamido macrocyclic ligands via an iterative design process in which oxidatively sensitive ligand moieties are identified and replaced.[1] Here we describe a subtle ligand design feature, the application of which has proved vital for obtaining an iron-based activator with a sufficiently long life to usefully activate H_2O_2 for oxidation in water from neutral to basic pH. The reactivity results demonstrate the potent oxidizing properties of the new activator system.



I



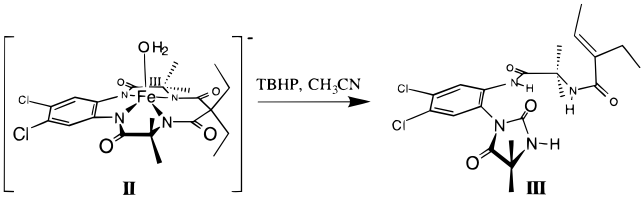
II

The two H_2O_2 activators compared in this study, **I** and **II**, can be prepared using procedures described in the literature.[6−8] The activators differ only in their respective six-membered chelate rings, wherein **I** contains a geminal dimethyl group while **II** contains a geminal diethyl group. In separate studies,[9] it was found that, in the presence of organic peroxides in CH_3CN, <10% of **II** underwent oxidative decomposition producing **III**. Examination of the structure of **III** suggested that this degradation was initiated by an H-atom abstraction from the methylene C−H bond of one of the two ethyl groups, a mechanism requiring the rate of degradation to be dependent upon the strength of the methylene C−H bond. Examples of intramolecular C−H bond activation of aliphatic hydrocarbon ligand groups can be found in copper and cobalt chemistry,[10−15] and in our rules for protecting ligands from oxidative decay.[1] We hypothesized that replacement of the ethyl groups with methyl groups would result in a longer-lived H_2O_2 activator; the primary C−H bonds of propane are 3 kcal·mol^{-1} stronger than the secondary C−H bonds of propane.[16,17] Thus, **I** was synthesized and a protocol for comparing the two activator lifetimes was developed upon the basis of the technologically important[18] process of dye bleaching in aqueous solution.

Table 1. Dye Bleaching Reactions Using $[Et_4N]I$ in H_2O

	bleaching time/s (activator concn/μM; T/°C)[a,b,c]		
dye (λ_{max}/nm)[e]	pH 7.4	pH 10	**IV**[d]
PC (600)	40 (0.43; 25)	40 (0.087; 25)	98[f]
Chicago sky blue 6b (590)	500 (1.74; 35)	70 (0.087; 25)	
Evans blue (596)	300 (0.43; 35)	15 (0.43; 35)	
Acid orange 8 (488)	slow (1.1; 35)	60 (1.1; 35)	
Acid red 97 (496)	7200 (0.43; 35)	160 (0.43; 35)	
Acid blue 25 (604)	3000 (0.43; 35)	20 (0.43; 35)	
Acid blue 29 (592)	1600 (1.1; 35)	30 (0.22; 35)	
Acid blue 92 (562)	40 (0.43; 35)	20 (0.43; 35)	
Direct violet 51 (550)	1600 (0.43; 35)	1600 (0.43; 35)	
Direct red 81 (554)	700 (0.87; 35)	900 (0.43; 35	44
Calmagite (582)	400 (0.43; 25)	<20 (0.43; 25)[g]	10.2[h]
Rhodamine b (554)	1800 (0.43; 35)	1800 (0.43; 35)	2.9

[a] Bleaching time is defined to be the time at which both $A \leq 0.1$ and the slope of the A vs time curve approaches zero for a chosen $\lambda_{max}{}^{d}$. [b] 4−8 mM H_2O_2 as oxidant. [c] pH 7.4 buffer; pH 10 buffer. [d] % bleaching in 30 mm for 18.9 μM $[Mn^{III}TPP]^+$ with imidazole as axial ligand. [e] λ_{max} was the wavelength used to determine the bleaching time. [f] In the absence of the Mn catalyst, 90% bleaching of the dye was observed. [g] In the absence of catalyst, calmagite was bleached within 250 s at pH 10. [h] This value is for Eriochrome black T, an analogue of calmagite.



Since most commercially available azo and quinone dyes are marketed as mixtures (40−50% purity), the marketed-pure pinacyanol chloride (PC) was chosen for initial study. The efficacy of **I** as a H_2O_2 activator for bleaching PC can be seen from the data of Figure 1. In the experiments, **I** at various concentrations, PC (12 μM), and carbonate buffer (pH 10) were combined and stirred in a quartz cuvette. Then, H_2O_2 (1.2 μL of standardized 30% H_2O_2; 3.9 mM) was added and the decrease in the PC absorption band at $\lambda_{max} = 600$ nm ($A_{600\ nm}$) was monitored as a function of time. For example, at 17 nM **I**, a **I**-to-PC ratio of 1:706, PC bleaching was complete in about 3 min. PC was also bleached in pH 7.4 solutions (phosphate buffer); $A_{600\ nm}$ was reduced to 0 in less than 1 min at 0.4 μM **I**. Under conditions similar to those used in Figure 1, neither $[NH_4]_2Fe[SO_4]_2\cdot 6H_2O$ (0.64 μM) nor $[NH_4]Fe[SO_4]_2\cdot 12H_2O$ (1.97 μM) nor the metal ion sequestering agent Dequest 2066[19] (4 ppm, Monsanto) altered the bleaching rate of PC.

Comparative activator longevity experiments were performed

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[1] Collins, T. J. *Acc. Chem. Res.* **1994**, *27*, 279.

[2] Grinstaff, M. W.; Hill, M. G.; Labinger, J. A.; Gray, H. B. *Science* **1994**, *264*, 1311.

[3] Chang, C. K.; Ebina, F. *J. Chem. Soc., Chem. Commun.* **1981**, 778.

[4] Sorokin, A.; Séris, J.-L.; Meunier, B. *Science* **1995**, *268*, 1163.

[5] Hage, R.; Iburg, J. E.; Kerschner, J.; Koek, J. H.; Lempers, E. L. M.; Martens, R. J.; Racherla, U. S.; Russell, S. W.; Swarthoff, T.; van Vliet, R. P.; Warnaar, J. B.; van der Wolf, L.; Krijnen, B. *Nature* **1994**, *369*, 637.

[6] Collins, T. J.; Powell, R. D.; Slebodnick, C.; Uffelman, E. S. *J. Am. Chem. Soc.* **1991**, *113*, 8419.

[7] Bartos, M. J.; Kidwell, C.; Kauffmann, K. E.; Gordon-Wylie, S. W.; Collins, T. J.; Clark, G. R.; Münck, E.; Weintraub, S. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1216.

[8] The synthesis and characterization of $[Et_4N]$**I** are found in the Supporting Information.

[9] Bartos, M. J.; Gordon-Wylie, S. W.; Fox, B. G.; Wright, L. J.; Weintraub, S. T.; Kauffmann, K. E.; Munck, E.; Kostka, K. L.; Uffelman, E. S.; Rickard, C. E. F.; Noon, K. R.; Collins, T. J. *Coord. Chem. Rev.*

[10] Reinaud, O. M.; Theopold, K. H. *J. Am. Chem. Soc.* **1994**, *116*, 6979.

[11] Mahapatra, S.; Halfen, J. A.; Wilkinson, E. C.; Que, L., Jr.; Tolman, W. B. *J. Am. Chem. Soc.* **1994**, *116*, 9785.

[12] Itoh, S.; Kondo, T.; Komatsu, M.; Ohshiro, Y.; Li, C.; Kanehisa, N.; Kai, Y.; Fukuzumi, S. *J. Am. Chem. Soc.* **1995**, *117*, 4714.

[13] Hikichi, S.; Komatsuzaki, H.; Kitajima, N.; Akita, M.; Mukai, M.; Kitagawa, T.; Moro-oka, Y. *Inorg. Chem.* **1997**, *36*, 266.

[14] Allen, W. E.; Sorrell, T. N. *Inorg. Chem.* **1997**, *36*, 1732.

[15] Wang, Y.; DuBois, J. L.; Hedman, B.; Hodgson, K. O.; Stack, T. D. P. *Science* **1998**, *279*, 537.

[16] Wayner, D. D. M.; Griller, D. *Advances in Free Radical Chemistry*; Wayner, D. D. M., Griller, D., Ed.; JAI Press: Greenwich, CT, 1990; Vol. 1.

[17] Castelhano, A. L.; Griller, D. *J. Am. Chem. Soc.* **1982**, *104*, 3655.

[18] Vickerstaff, T. *The Physical Chemistry of Dyeing*; Interscience Publishers Inc.: New York, 1954.

[19] Monsanto, Chemical Co. Publication No. WT8601.

S0002-7863(97)02891-6 CCC: $15.00

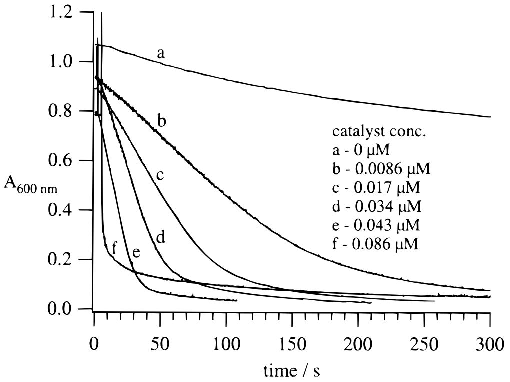

Figure 1. $A_{600\,\mathrm{nm}}$ vs time plot of the bleaching of a single 12 μM aliquot of pinacyanol chloride with **I** at the concentrations noted on the figure. Reaction conditions: pH 10; $T = 25$ °C; 3.9 mM H_2O_2.

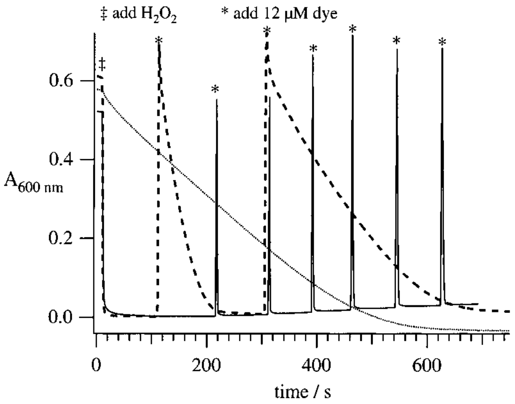

Figure 2. $A_{600\,\mathrm{nm}}$ vs time plot of the bleaching of a series of 12 μM aliquots of pinacyanol chloride using (···) 0.0 μM catalyst, single aliquot; (—) 0.43 μM **I**, seven aliquots; (- - -) 0.43 μM **II**, three aliquots. Reaction conditions: pH 10; $T = 35$ °C; 3.9 mM H_2O_2, 4 ppm Dequest 2066.

in a manner similar to the experiments shown in Figure 1 except that, following bleaching of the first aliquot of PC, additional PC aliquots (30 equiv relative to **I** or **II**) were added when the $A_{600\,\mathrm{nm}}$ reached 0 (Figure 2). A dramatic increase in bleaching longevity was observed for **I** compared with **II**. For example, at pH 10, the bleaching rate of PC is the same for **I** and **II** in the first cycle. However, with **II**, only one rapid bleaching cycle could be achieved. By the fourth bleaching cycle, only a small degree of enhancement over the background rate was observed, signaling that degradation of **II** was removing it from the activator pool. In contrast, after seven bleaching cycles (195 turnovers), bleaching remained extremely efficient for **I**; rapid dye oxidation could still be performed with **I** as the activator beyond 1 h. These results show that **I** is a potentially viable H_2O_2 activator for dye bleaching reactions under conditions where the substrate:catalyst ratio is moderately low while **II** is significantly less useful. At all pH's investigated, **II** was found to be short-lived compared to **I**.

The superior longevity of **I** compared to **II** as a H_2O_2 activator in the presence of H_2O_2 and absence of substrate is shown in Figure 3. In this case, **I** (4.02 μM) or **II** (4.04 μM) and Dequest (4 ppm) were combined and stirred in pH 10 buffer (3.0 mL, 20 °C), then H_2O_2 (2 μL, 8.11 M) was added, and the changes in $A_{454\,\mathrm{nm}}$ were monitored. There is no residual absorption from H_2O_2 in this spectral region. Higher concentrations of **I** and **II** compared to those used for the dye bleaching studies (Figures 1 and 2) were used in order to have sufficient absorbance at 454 nm. For both complexes, a rise in absorption occurs immediately following H_2O_2 addition, indicating the formation of a new species (we are currently pursuing the nature of this species). This rise is then followed by slow decay in absorbance for the species derived from **I** and a much more rapid decay for that based on **II** (a detailed kinetic study of the decomposition process of **II** is in progress). After approximately 200 s, the species from **II** appears to be destroyed while that from **I** still has residual absorbance at 454 nm after 2 h (data not shown). Peroxide was still present in both cases at 900 s as determined by the formation of iodine upon addition of iodide.

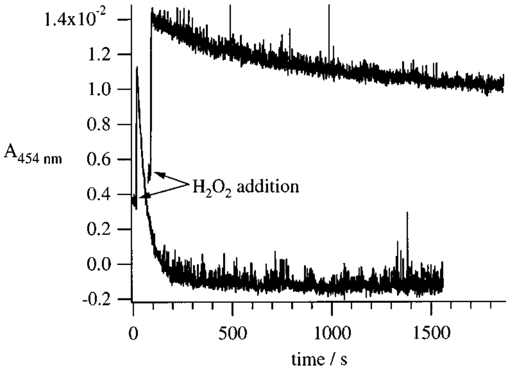

Figure 3. $A_{454\,\mathrm{nm}}$ vs time plots for the reaction of **I** (4.02 μM) (upper trace) and **II** (4.04 μM) (lower trace) with 5.4 μM H_2O_2 at pH 10 ($T =$ 20 °C, 4 ppm Dequest 2066).

Complex **I** is a highly effective H_2O_2 activator for bleaching of all dyes we have studied to date. The bleaching rate is dye-dependent, which is likely a consequence of the different oxidative robustness of each individual dye.[18] Many of the azo- and quinone-based dyes at both pH 7.4 and 10 could be bleached in much less than 15 min at sub-micromolar activator concentrations (Table 1). The bleaching of some of the dyes used here has been investigated in CH_3OH/H_2O using the Mn(III) TPP imidazole complex, **IV**, as the activator (18.9 μM) and sodium perborate (2.45 mM).[20] While it is difficult to make direct comparisons with the chemistry of **I** and **II**, the bleaching rates of this system are also shown in Table 1 as the percent bleaching of the dye after 30 min. In all cases, the **I**/H_2O_2 system effects much more rapid bleaching than the Mn system. Other azo dyes have been bleached using oxidatively stabilized, water-soluble Fe(III) porphyrins in combination with peroxide-containing detergents.[21,22] While the iron porphyrin complexes do bleach the dyes at moderate rates, their lifetimes are much less than that of the **I**/H_2O_2 system. Finally, Mn(III) complexes with TACN ligands have been shown to be efficient H_2O_2 activators for the oxidation of polyphenolic compounds and alkenes.[5]

This study reveals that the change of peripheral ethyl for methyl ligand substituents in the six-membered ring of our macrocyclic tetraamides is important for obtaining long-lived and useful homogeneous H_2O_2 activators. This is a subtle feature of ligand design, and the impact that it has on the utility of the H_2O_2 activator was unexpected. Because **I** efficiently activates H_2O_2 at very low complex and low H_2O_2 concentrations and also has a significant lifetime, it should be effective for a variety of valuable oxidation processes. We are currently working to identify metal complex intermediates in the oxidation processes. We are also examining a broad range of fields of use and are working toward the preparation of even more oxidatively robust catalysts.

Acknowledgment. This work was supported by the National Institutes of Health (GM44867-05) and the National Science Foundation (CHE9319505 and CHE9612990).

Supporting Information Available: The synthesis and characterization of [Et_4N]**I** (1 page, print/PDF). See any current masthead page for ordering information and Web access instructions.

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[20] Bhirud, R. G.; Srisankar, E. V.; Narayan, K. S. *Proc. Indian Acad. Sci.* **1991**, *103*, 83.

[21] Johnston, J. P.; Tate, J. R. U.S. Patent 4 077 768, 1978.

[22] Thoen, C. A. J. K.; Fredj, A.; Lebeque, R. European Patent 553 608 A1, 1993.