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Sulfide oxygenation by *tert*-butyl hydroperoxide with mononuclear (Me_3TACN)Mn catalysts

Julia E. Barker and Tong Ren*

Department of Chemistry, University of Miami, Coral Gables, FL 33146, USA

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Abstract—Mononuclear (Me_3TACN)MnX_3 compounds, where X is Cl^-, Br^-, or N_3^-, and Me_3TACN is 1,4,7-*N*,*N*′,*N*″-trimethyl-1,4,7-triazacyclononane, have been tested for catalyzing both sulfide oxygenation and styrene epoxidation by *tert*-butyl hydroperoxide (TBHP) and display turnover frequencies (TOF) up to 200 h^{-1} at room temperature. Sulfoxides or sulfones may be produced selectively by varying reaction conditions. Product distribution from the oxygenation reactions of ethyl phenyl sulfide, 2-chloroethyl phenyl sulfide, and styrene is consistent with a mechanism involving an early single-electron transfer (SET) step.

Catalytic oxygenation of organic sulfides is a multifaceted area that impacts various fields including the pharmaceutical industry and the petroleum industry (desulfurization).[1–3] There is a continued interest in selective oxygenation leading to sulfoxides,[4] sulfones, and epoxides,[5,6] and novel methodologies for allylic oxidation[7] as the products from these reactions are useful intermediates and products in organic synthesis. Consequently, catalytic means of oxo-transfer to organic sulfides and olefins under mild conditions are sought utilizing inexpensive and environmentally friendly oxygen donors such as O_2, H_2O_2, and ^{t}BuOOH (TBHP). A number of catalytic systems, both organic and inorganic, facilitating H_2O_2 activation have been reported and reviewed by Lane and Burgess.[5] In contrast, fewer catalysts facilitating oxygenation of organic sulfides by TBHP have been reported since TBHP is an oxidant difficult to activate due to its size and electron donation from its *tert*-butyl group. Among these examples, MeReO(mtp)PPh_3 (mtp = 2-(mercaptomethyl)thiophenol) by Espensen and co-workers catalyzes the oxygenation of methyl phenyl sulfide with a remarkable turnover frequency (TOF) of 100 at room temperature.[8] Other catalysts effective in activating TBHP include complexes of a $[Mn_4O_4]^{6+}$ cubane core,[9] polyoxometalates,[10] titanium-based catalysts,[4] Cu-salen complexes,[11] and $VO(acac)_2$.[12] The dimanganese compound $[(Me_3TACN\text{-}Mn)_2(\mu\text{-}O)(\mu\text{-}OAc)_2]^{2+}$ (Me_3TACN is 1,4,7-*N*,*N*′,*N*″-trimethyl-1,4,7-triazacyclononane) was utilized to promote sulfide oxygenation by TBHP in microemulsions with a TOF around 4.[12]

In addition to the activation of TBHP, chemical selectivity is also an intriguing aspect of sulfide oxygenation chemistry. Organic sulfide oxygenation occurs sequentially first to sulfoxide, which is followed by the formation of sulfone (Eq. 1). Often, catalysts that are capable of transferring oxygen to sulfides may not be selective for sulfoxide production, namely significant sulfone formation may occur prior to the complete consumption of sulfide, as the reactivity of sulfides and sulfoxides are inherently similar.

$$RSAr \rightarrow RS(O)Ar \rightarrow RS(O)_2Ar \tag{1}$$

Previously, we investigated the efficacy of both manganese complexes $\{[(Me_3TACN)Mn]_2(\mu\text{-}O)_3\}^{2+}$ and $\{[(Me_3TACN)Mn]_2(\mu\text{-}O)(\mu\text{-}O,O'\text{-}O_2CMe)_2\}^{2+}$, and polyoxo ion $[\gamma\text{-}SiW_{10}O_{34}(H_2O)_2]^{4-}$ in catalyzing organic sulfide oxygenation by H_2O_2.[13,14] In this contribution, we describe the oxo-transfer to both organic sulfides and olefins from TBHP promoted by the (Me_3TACN)MnX_3 type compounds with X as Cl^- (**A**), Br^- (**B**), or $(N_3)^-$ (**C**) as seen in Figure 1.[15]

Organic sulfides utilized for reactivity study are phenyl sulfide (PPS), methyl phenyl sulfide (MPS), ethyl phenyl

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Keywords: Organic sulfide; Epoxidation; *tert*-Butyl hydroperoxide; Catalytic oxygenation; Mn–Me_3TACN compounds.

* Corresponding author. Current address: Department of Chemistry, Purdue University, West Lafayette, IN 47907, USA. Tel.: +1 3052846617; fax: +1 3052841880; e-mail: tren@purdue.edu

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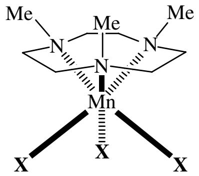


Figure 1. Schematic representation of mononuclear Mn synthesis where X = Cl^- (**A**), Br^- (**B**), or $(N_3)^-$ (**C**).

sulfide (EPS), and 2-chloroethyl phenyl sulfide (CEPS). Results of their TBHP oxygenation reactions facilitated by either **A**, **B**, or **C** are summarized in Table 1. Both **A** and **B** are capable of promoting either sulfoxide or sulfone formation by varying the reaction time and equivalents of TBHP added under ambient conditions. As shown by the product evolution during the course of PPS oxygenation in Figure 2, profiled with GC–MS analysis at 15 min intervals, a true stepwise progression occurs with quantitative formation of phenyl sulfoxide within 1 h, followed by a much slower conversion to sulfone.

Further analysis of the oxygenation of PPS with **A** revealed that the use of 8 equiv of TBHP yielded sulfone quantitatively in 1 h (Table 1, entry 3), which corresponds to a TOF of 200. Oxygenation of PPS with 2 equiv of TBHP resulted in sulfoxide (89%) only in 7 h (entry 1), also indicating that both the reaction rate and product distribution are highly dependant on oxidant concentration. MPS could also be converted to either sulfoxide or sulfone in a stepwise fashion using **A** in nearly quantitative yield, although the conversion was much slower than PPS with the highest TOF of 13 only (entry 4).

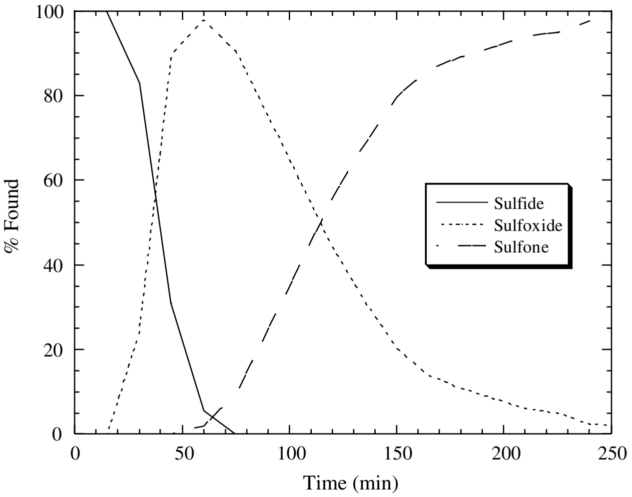


Figure 2. PPS conversion to sulfoxide then sulfone by TBHP with $(Me_3TACN)MnCl_3$ (data are the average of 3 runs).

Interestingly, an opposite trend in rates was observed with $MeReO(mtp)PPh_3$ by Espensen: a TOF of 100 was found for MPS, while that with PPS was only 20.[8]

Analysis of both EPS and CEPS revealed the presence of large amounts of disulfide products (entries 5 and 6) that were absent in the cases of PPS and MPS. Clearly, disulfide products are only produced from sulfides with acidic α-protons, and their formation is indicative of a sulfenium radical intermediate, as discussed below.[16] The monomeric catalysts **A** and **B** yield larger amounts of disulfide product than dimanganese catalysts in the presence of the same substrate and H_2O_2.[13] Noteworthy is

Table 1. Oxygenation of organic sulfides with $(Me_3TACN)MnX_3$ complexes using TBHP[a]

Entry	Sulfide	Catalyst	TBHP (equiv)	Reaction time (h)	Sulfide	Sulfoxide	Sulfone	Other[b]	TOF[c]
1	PPS	**A**	2	7	11	89	0	0	13
2	PPS	**A**	4	1	0	99	1	0	101
				4	0	2	98	0	50
3	PPS[d]	**A**	8	1	0	0	100	0	200
4	MPS	**A**	4	7	9	90	1	0	13
				24	0	13	87	0	8
5	EPS	**A**	4	1.5	1	2	70	27	95
				3	0	0	99	1	66
6	CEPS[e]	**A**	4	6	41	25	0	34	4
				24	10	11.0	32	47	3
7	PPS	**B**	4	5	13	87	0	0	17
8	PPS[d]	**B**	8	1.5	1	99	0	0	66
				24	0	6	94	0	8
9	PPS	**C**	4	2	>99	Trace	0	0	0
10	PPS[f]	$MnCl_2 + Me_3TACN$	4	24	≫99	Trace	0	0	0

[a] Reaction conditions: 2 mmol sulfide, 17 mL CH_3CN, 2 mL H_2O, indicated amount of TBHP added from 70% aqueous solution. Reaction initiated by the addition of 1 mol% (20 μmol) catalyst. TBHP concentration (8.24 M) established with iodometric analysis. All reactions were performed at room temperature (23 ± 2 °C). Aliquots of the reaction mixtures were combined with an aliquot of 1 M NaOH and neutralized with 1 M HCl before GC–MS analysis. Product identifications were verified by their MS in accordance with the NIST database.[23]

[b] Disulfides (PhSSPh) and their respective oxidation products: PhS(O)S(O)Ph or $PhS(O)_2SPh$.

[c] Turnover frequency (h^{-1}) = $\{[RR'SO] + 2[RR'SO_2]\}/\{[Cat] * \text{time (h)}\}$.

[d] CH_3CN was reduced to 16 mL when 16 mmol TBHP was present.

[e] Sulfoxide and sulfone product detected was identified as phenyl vinyl sulfoxide and phenyl vinyl sulfone.

[f] In situ reaction: 2 mmol sulfide, 17 mL CH_3CN, 8 mmol TBHP added from 70% aqueous solution and 0.05 mmol Me_3TACN. Reaction initiated by the addition of 0.04 mmol $MnCl_2$.

the product identity from CEPS oxygenation: phenyl vinyl sulfoxide or phenyl vinyl sulfone, the same elimination products found with CEPS in a previous study with dimanganese complexes supported by Me_3TACN.[13]

Catalyst **B** resulted in lower TOFs than **A** under the same conditions (entries 7 and 8). Compound **C** was catalytically inactive (entry 9). A reaction with catalyst generated in situ was attempted through the addition of free ligand and $MnCl_2$ under similar reaction conditions, but only yielded a trace amount of oxygenation product (entry 10), and the formation of MnO_2 appeared prevalent.

Additives, often weak bases, are known to enhance the rate of epoxidation reactions catalyzed by metal species, and a list of common additives can be found in the survey by Lane and Burgess.[5] However, none of additives from Burgess's list resulted in significant rate enhancement in the TBHP oxygenation reaction of PPS catalyzed by **A**. Instead, several of which were found to severely retard the reaction including acetate, tartrate, oxalate, ascorbate, and benzoate. Other additives tested with little effect on the reaction rate include: benzoic acid/imidazole (1:1), benzimidazole, KCl, and NH_4Cl. Co-additive stock solutions were maintained at neutral pH by addition of either KOH or HCl before introduction to the reaction mixture.

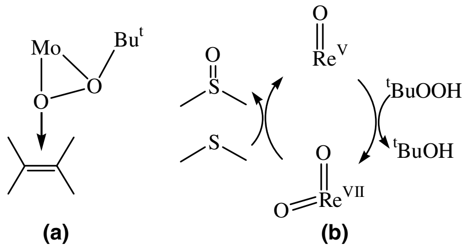
Olefins and organic sulfides often exhibit similar reactivity toward an oxygenation system: namely sulfides can be converted to sulfoxides/sulfones under the conditions used for olefin epoxidation, and vice versa. Hence, the oxygenation of styrene was also investigated using 1 mol % of **A** in the presence of TBHP. Nearly quantitative conversion of styrene to its epoxide was achieved in 45 min with 10 equiv of TBHP (TOF = 130), as may be seen in Table 2 (entry 1). The remaining 4% product was identified as benzaldehyde, which was previously identified as a product of double bond cleavage by Neumann and co-workers.[17] Interestingly, upon the addition of 0.5 mol % sodium oxalate to this system, no epoxide was detected (entry 2).

Table 2. Reaction of styrene with $(Me_3TACN)MnCl_3$ and TBHP

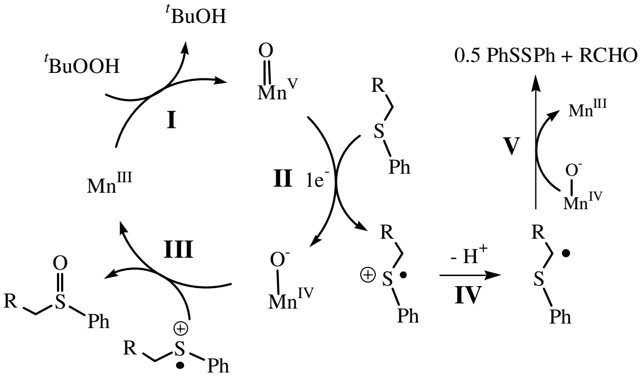
Entry	Co-additive (mol %)	Styrene	Epoxide	Other	TOF
1	None	0	96	4	133
2	Oxalate (0.05)	0	none	100	NA

Reaction conditions: 2 mmol styrene, 10 mL CH_3CN, and 10 equiv TBHP added from 70% aqueous solutions. Reaction initiated by the addition of 1% catalyst. TBHP concentration established by iodometric analysis.

Two mechanisms have been proposed for metal-catalyzed TBHP oxygenation reactions (Scheme 1): the direct oxo-transfer from an η^2-alkyl peroxide to olefin mediated by a Mo^{VI} center (concerted mechanism),[18,19] and oxo-transfer from TBHP to a Re^V center and subsequent oxo-transfer to the sulfur center (stepwise mechanism).[8] While both mechanisms are plausible for the oxygenation of PPS and MPS, neither could account for the formation of disulfides observed for EPS and CEPS.



Scheme 1. Two oxo-transfer mechanisms proposed in literature: (a) concerted, (b) stepwise.



Scheme 2. Plausible pathway for TBHP oxygenation of sulfide with $(Me_3TACN)Mn$ complexes.

To properly account for the formation of disulfides, we offer a revised oxo-transfer mechanism shown in Scheme 2, which is delineated in the ensuing discussion. Similar to the case of $MeReO(mtp)PPh_3$, the sequence begins with the direct oxo-transfer from TBHP to Mn center to yield a $(Me_3TACN)Mn^V{=}O$ intermediate, which was detected with ESI mass spectrometry recently.[20] In the second step (**II**), the $(Me_3TACN)Mn^V{=}O$ species serves as a one-electron oxidizer to convert sulfide to the corresponding sulfenium radical, a process commonly known as SET (single-electron transfer) reaction. The resultant sulfenium combines with $(Mn^{IV}–O)^{1-}$ subsequently (**III**, oxygen rebound) to yield the corresponding sulfoxide that is observed in each oxygenation reaction. Sulfenium as the reaction intermediate has been invoked in rationalizing sulfide oxygenation by P-450[16] and ruthenium oxo species.[21] In the presence of an acidic α-hydrogen, as in the cases of CEPS and EPS, sulfenium radical may react via an alternative pathway: it deprotonates to yield a carbon-centered radical (step **IV**), which is converted to aldehyde and disulfide on oxygen rebound (step **V**). Also noteworthy is the formation of benzaldehyde byproduct during styrene epoxidation, which is the signature of radical intermediate(s). Hence, it is plausible that the TBHP epoxidation of styrene follows a similar reaction pathway involving a SET step parallel to the oxygenation of sulfides. Reminiscent of Scheme 2, a radical intermediate has been postulated for the Mn^{III}-salen catalyzed Jacobsen–Katsuki epoxidation.[22]

We have demonstrated that mononuclear (Me$_3$-TACN)MnX$_3$ compounds are capable of catalytic oxo-transfer when X = Cl$^-$ (**A**) or Br$^-$ (**B**) in the presence of TBHP and display high TOFs with the use of non-chlorinated solvents. Sulfoxide or sulfone products may be quantitatively produced for both PPS and MPS. Styrene oxide is produced in nearly quantitative yield in the presence of **A** and TBHP. In addition, the expected oxygenation products, oxygenation of EPS, and CEPS also resulted in disulfide products, which imply the presence of a sulfenium radical intermediate.

Acknowledgments

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