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Facile oxygenation of organic sulfides with H_2O_2 catalyzed by Mn–Me_3TACN compounds

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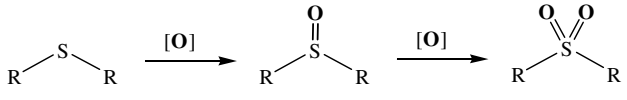
Abstract—Two binuclear Mn–Me_3TACN (Me_3TACN is 1,4,7-*N*,*N*′,*N*″-trimethyl-1,4,7-triazacyclononane) compounds catalyze the oxygenation of organic sulfides utilizing H_2O_2 under ambient conditions. Both phenyl sulfide and ethyl phenyl sulfide were converted to the corresponding sulfones and chloroethyl phenyl sulfide proceeds to its elimination product of phenyl vinyl sulfone.

Organic sulfides and their oxygenated derivatives are of interest as either synthetic intermediates or final products, and their catalyzed syntheses under mild conditions are currently topical.[1] In addition, oxygenation of the sulfur centre plays a significant role in decontamination of sulfur-containing chemical warfare agents such as VX and mustard gas (HD), where a current protocol employs copious amounts of bleach.[2] Oxygenation of organic sulfides occurs stepwise: sulfide to sulfoxide and sulfoxide to sulfone (Scheme 1). Ability to limit the oxygenation at sulfoxide formation is also highly desired in both organic synthesis and mustard gas decontamination. In order to achieve fast decontamination/detoxification of VX and HD, catalysts capable of accelerating sulfide oxygenation with *simple oxidants* such as H_2O_2, ^{t}BuOOH and O_2 under *ambient conditions* remain highly desired.[2,3] Notable recent examples of catalytic systems include utilizing H_2O_2 with peroxycarbonate,[4] methyloxorhenium,[5] tungstate and molybdate[6] and aerobic oxygenation by various metal complexes.[7]

We are interested in the possibility of catalytic oxygenation of organic sulfides by H_2O_2 promoted by two manganese compounds supported by Me_3TACN (Fig. 1), $[(Me_3TACN\text{-}Mn)_2(\mu\text{-}O)_3](PF_6)_2$ (**A**) and $[(Me_3TACN\text{-}Mn)_2(\mu\text{-}O)(\mu\text{-}O,O'\text{-}O_2CMe)_2](PF_6)_2$ (**B**), where Me_3TACN is 1,4,7-*N*,*N*′,*N*″-trimethyl-1,4,7- triazacyclononane.[8] Compound **A** was shown to be an excellent catalyst for olefin epoxidation by H_2O_2 in aqueous media.[9] It was established subsequently that a mixture of Mn^{2+} salt and Me_3TACN in approximate 1:1 molar ratio resulted in remarkable TOF (turnover frequency) of epoxidation in the presence of a co-catalyst such as oxalate and ascorbate in aqueous solutions.[10] Efficacy of **A** in promoting the conversion of organic sulfides to sulfones was first demonstrated using periodic acid as the oxygen donor with the best TOF around 180.[11]



Scheme 1. Oxygenation of organic sulfide.

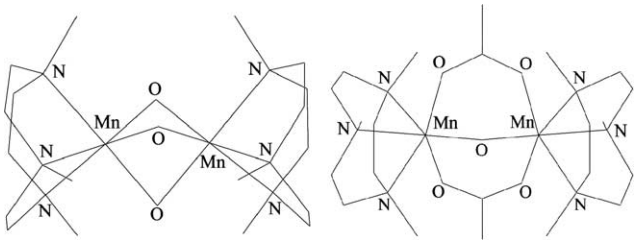


Figure 1. Structural representation of catalysts **A** (left) and **B** with counter ions omitted; based on data retrieved from Cambridge Structure Database.

Keywords: Organic sulfide; Catalytic oxygenation; Mn–Me_3TACN complexes; Hydrogen peroxide.
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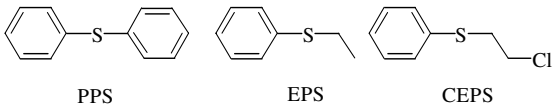


PPS EPS CEPS

Scheme 2. Organic sulfide substrates.

Subsequent study of methyl phenyl sulfide oxygenation using **A** and H_2O_2 resulted in an excellent TOF of 570.[12] In addition, enhancement of catalytic activity of **A** in the presence of carboxylic buffers was demonstrated for benzylic oxidation of aromatics,[13] which prompted us to consider catalyst **B** (Scheme 2), a compound containing stoichiometric amounts of carboxylate, as a possible alternative to **A**.

Three organic sulfides were selected for the assessment of oxygenation potency of catalytic systems: phenyl sulfide (PPS), ethyl phenyl sulfide (EPS) and 2-chloroethylphenyl sulfide (CEPS) (Scheme 2), the latter of which is often used as the stimulant of mustard gas.[2,14] The reaction progress was monitored through GC–MS (Table 1) and product identities were authenticated using ^{1}H NMR spectra. At indicated times, the reaction was stopped by the addition of NaOH, converting the catalyst to MnO_2.

Both compounds **A** and **B** effectively catalyze sulfide oxygenation with H_2O_2 in the absence of co-catalysts (entries 1, 2, 5, 7, 9 and 11), and the TOFs determined for **A** are comparable with that reported for methyl phenyl sulfide.[12] Amazingly, the addition of oxalate/oxalic acid (1:1) as the co-catalyst resulted in up to 40-fold increase in the TOF for both **A** (entries 1 vs 2; 5 vs 6; and 9 vs 10) and **B** (entries 3 vs 4; 7 vs 8; and 11 vs 12). In contrast to catalytic epoxidation,[10] the presence of ascorbate did not accelerate the oxygenation of sulfides by either **A** or **B** (entries 14 and 15), but enhanced the rate of H_2O_2 disproportionation.

PPS and EPS were oxidized from the sulfide to sulfoxide to sulfone sequentially, though disulfide oxidation products were detected for the latter substrate. For CEPS, the final product was identified as phenyl vinyl sulfone upon reaction completion and addition of NaOH. Without NaOH, this product was also formed along with minimal disulfide oxidation products. It is known that disulfides may be formed through catalytic reactions due to the presence of acetic α-hydrogens that, upon abstraction, may be followed by the fusion of the sulfide centres.[15] Thus, if hydrogen abstraction occurs with CEPS, chloride groups may easily leave creating its respective elimination product. Phenyl vinyl sulfone was shown to be stable under the conditions of ours and Barton's catalytic reactions.[11] Noting that efficient epoxidation was achieved using catalyst generated from mixing free Me_3TACN and Mn(II) salt in situ, we also tested sulfur oxygenation under similar conditions (entry 16), which did not result in detectable amount of sulfoxide.

Despite remarkable successes in catalytic olefin epoxidation reactions, the exact mechanism of H_2O_2 activation by Mn–Me_3TACN complexes remains undetermined. We speculate that one of two possible intermediates in Scheme 3 is responsible for an electro-

Table 1. Oxidation products of organic sulfides with H_2O_2 in the presence of either **A** or **B**[a]

Entry	Substrate	Catalyst	Oxalate present	Reaction time	Sulfide	Sulfoxide	Sulfone	Other[b]	TOF[c]
1	PPS	**A**	None	4 h	0	0	100	0	333
2	PPS	**A**	Yes	15 min	0	0	100	0	5330
3	PPS	**B**	None	4 h	<1	50	50	0	250
				6 h	0	26	74	0	190
4	PPS	**B**	Yes	30 min	0	0	100	0	2660
5	EPS	**A**	None	5 h	0	11	70	19	200
				7 h	0	12	78	11	160
6	EPS	**A**	Yes	20 min	0	0	100	0	4000
7	EPS	**B**	None	4 h	32	25	23	20	120
8	EPS	**B**	Yes	30 min	0	0	100	0	2660
9	CEPS	**A**	None	8 h	10	0	83	7	140
10	CEPS	**A**	Yes	20 min	0	0	100	0	4000
11	CEPS	**B**	None	7 h	52	0	39	13	74
				16 h	20	0	38	42	32
12	CEPS	**B**	Yes	25 min	0	0	100	0	3200
13[d]	CEPS	**A**	Yes	15 min	4	1	74	21	4000
				30 min	0	0	98	2	2600
14	PPS	**A**	Yes[e]	2 days	<100	Trace	0	0	0
15	EPS	**B**	Yes[e]	10 min	100	0	0	0	0
16	PPS	**A**[f]	No	45 min	100	0	0	0	0

[a] Reaction conditions: 100 μmol sulfide, 0.700 mL CH_3CN, 0.0015 equiv catalyst, 0.0023 M oxalic acid–oxalate 1:1 if indicated. Reaction started by the addition of 100 μL of 12.0 M H_2O_2 in H_2O (concentration established with iodometric analysis). All reactions were performed at room temperature (23 ± 2 °C). Percentages determined by GC–MS. Results depicted are an average of two runs.

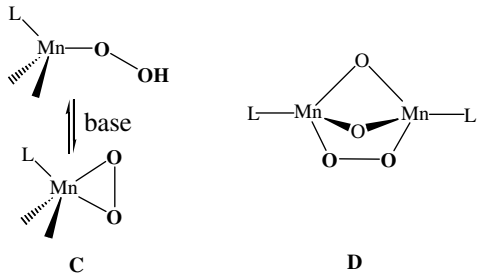
[b] Disulfides (PhSSPh) and their respective oxidation products (PhS(O)SPh, or PhS(O)S(O)Ph, $PhS(O)_2SPh$).

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

[d] Did not use NaOH to kill catalyst, depicted from a single run of each.

[e] 0.0023 equiv of 1:1 mixture of ascorbic acid–ascorbate used as the co-catalyst; reaction mixture analyzed by ^{1}H NMR.

[f] In situ reaction from adding 0.0042 equiv Me_3TACN and 0.003 equiv $MnCl_2$ to 100 μmol sulfide in 0.700 mL CH_3CN.



Scheme 3. Catalytic intermediates **C** and **D**; L = Me_3TACN.

philic activation of hydrogen peroxide. In order to ascertain which mechanism is operative, further kinetic studies are necessitated.

In conclusion, we have demonstrated the facile oxygenation of organic sulfides under mild conditions. Both catalysts **A** and **B** convert organic sulfides to their respective sulfoxides, and then to their sulfones at comparable efficiencies. However, catalytic oxygenation of CEPS, the mustard gas simulant, resulted in significant production of the corresponding vinyl sulfone, an analogous end product generated for mustard gas from the current decontamination protocol by using household bleach.[2] This result suggests that our catalytic conditions may be used to decontaminate mustard gas. Contrary to the catalytic epoxidation reactions, Mn/Me_3TACN in situ mixture did not catalyze sulfide oxygenation, illustrating both the significance of using well-defined Mn-compounds and subtle mechanistic differences between epoxidation and sulfide oxygenation.

Acknowledgements

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