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LETTERS

Homogeneous *cis*-dihydroxylation and epoxidation of olefins with high H_2O_2 efficiency by mixed manganese/activated carbonyl catalyst system

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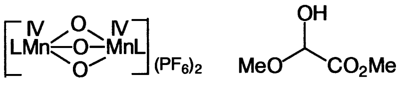
Abstract—The use of $[Mn_2O_3(tmtacn)_2](PF_6)_2$ (tmtacn = 1,4,7-trimethyl-1,4,7-triazacyclononane) in combination with glyoxylic acid methylester methyl hemiacetal (GMHA) results in a highly active and hydrogen peroxide efficient catalyst for the epoxidation of olefins as well as the first homogeneous catalytic *cis*-dihydroxylation system with H_2O_2 and with turnover numbers up to 420.

For economic and environmental reasons catalytic olefin oxidations based on O_2 or H_2O_2 are preferred over traditional stoichiometric oxidations, e.g. epoxidation with peracids and *cis*-dihydroxylation with permanganate.[1] Several methods are available for catalytic epoxidation with aqueous H_2O_2 (notably Re-, W-, and Mn-based catalysts),[2] but high turnovers for *cis*-dihydroxylation are only achieved using Os.[3] However, the high cost and toxicity of Os hamper large scale application and provide a strong incentive to develop benign Fe- or Mn-based *cis*-dihydroxylation catalysts. Que et al. recently reported the first *cis*-dihydroxylation with H_2O_2 catalysed by a non-heme iron complex.[4] Although this system shows good *cis*-diol selectivities, turnover numbers (t.o.n.) are rather low (up until 22 t.o.n.).

Recently Mn complexes based on tmtacn were found to be highly active in catalytic oxidation,[5] but apart from high turnover, it is essential to develop catalytic systems that employ H_2O_2 very efficiently, as many Mn or Fe catalysts are known to be particularly effective in decomposition of H_2O_2.[6] This can be suppressed by working in acetone;[7] however, this solvent is not acceptable for large-scale applications because of the risk of formation of explosive cyclic peroxides. H_2O_2 decomposition by Mn–tacn complexes can be suppressed by addition of oxalate[8a] or ascorbic acid[8b] as co-catalysts, or by anchoring the tacn ligand to a solid support.[9] Significant amounts of *cis*-diols besides epoxides are formed during alkene oxidation with this heterogenised Mn catalyst.

Herein, we report efficient alkene oxidations with H_2O_2 catalysed by Mn–tmtacn **1**[10] in the presence of GMHA **2** (Fig. 1). Surprisingly, the latter not only strongly suppresses H_2O_2 decomposition by the Mn catalyst, but also imparts the first homogeneous catalytic *cis*-dihydroxylation activity to a Mn catalyst. Catalytic oxidations were performed by adding aqueous, 50% hydrogen peroxide (1.3 equiv. with respect to the sub-



1 **2**

Figure 1. L = 1,4,7-trimethyl-1,4,7-triazacyclononane.

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strate) in 6 h to a mixture of alkene, Mn–tmtacn catalyst (0.1 mol%), and GMHA (25 mol%) in MeCN at 0°C. Under these reaction conditions, the presence of GMHA as the co-catalyst enables high conversions with only a 30% excess of oxidant with respect to substrate (Table 1) and the H_2O_2 efficiency is drastically improved compared to previous Mn systems using excess of H_2O_2.[5] In most cases the conversions were also significantly higher than those obtained with oxalate as co-catalyst and 1.3 equiv. of H_2O_2 (for similar experiments with a larger excess of H_2O_2, see Ref. 8a).

In particular, styrene afforded a high yield of styrene oxide in the presence of GMHA, whereas the use of oxalate resulted in only modest conversion of styrene. When a mixture of GMHA (25 mol%) and oxalate (0.3 mol%) was used as the co-catalyst system, the epoxide yields even surpassed those obtained with the Mn/GMHA catalytic system, and high epoxide yields at complete conversion were obtained for the non-sterically hindered alkenes (Table 1, entries 1–3, 6, 8). Unexpectedly, substantial amounts of *cis*-diols were formed besides epoxides when *only* GMHA was present as the co-catalyst. The epoxide/*cis*-diol ratio depends strongly on the alkene structure. The highest amount of *cis*-diol was found for cyclooctene (entry 3), which afforded the *cis*-diol as the main product (42%, 420 t.o.n.) besides the epoxide (36%, 360 t.o.n.). Minor amounts of 2-hydroxycyclooctanone were also found due to overoxidation of the diol. The ring size of cycloalkenes has a profound influence on the epoxide/*cis*-diol ratio (entries 1–4). For these cyclic olefins, almost no *trans*-diol could be detected (ratio *cis*-diol/*trans*-diol >99.5/0.5). *cis*-Diol formation is also observed for aliphatic acyclic alkenes. Yields of diol are significantly lower for *trans*-2-hexene than from *cis*-2-hexene, but the epoxide/*cis*-diol ratio was similar for both substrates. The aryl-substituted alkenes (entries 7, 8) yield epoxide nearly exclusively under these conditions. Limited *cis*/*trans* isomerisation is observed in the epoxide formation of *cis*-2-hexene. The *cis*/*trans* isomerisation points to epoxidation via a Mn oxo species, with formation of epoxides from C-centred radical intermediates with a lifetime sufficient for some C–C bond rotation prior to reaction to the epoxide.[12] In line with this mechanism, olefins that form a relatively long-lived radical intermediate, such as *cis*-stilbene, show substantial loss of configuration in epoxide. No diols were formed on replacing the substrate by epox-

Table 1. Oxidation of selected olefins by H_2O_2 with catalyst **1**[11]

Entry	Substrate	Conversion (%)[e]			Product[d]	Turnover number (t.o.n.)[e]		
		Additive: GMHA[a] (**2**)	Additive: **2**+oxalate[b]	Additive: oxalate[c]		Additive: GMHA[a] (**2**)	Additive: **2**+oxalate[b]	Additive: oxalate[c]
1	Cyclopentene	97	100	92	Epoxide	610	860	770
					cis-Diol	260	0	0
					Cyclopentenone	80	10	100
2	Cyclohexene	88	100	73	Epoxide	590	820	610
					cis-Diol	90	0	0
					2-Cyclohexenone	80	80	70
3	Cyclooctene	90	100	52	Epoxide	360	840	410
					cis-Diol	420	60	0
					2-HO-cyclooctanone	220	80	0
4	Norbornylene	95	88	59	*exo*-Epoxide	540	530	360
					exo-*cis*-Diol	180	60	0
5	*trans*-2-Hexene	77	93	37	*trans*-Epoxide	210	550	240
					cis-Epoxide	50	30	0
					RR/*SS*-Diol	150	90	0
					RS/*SR*-Diol	0	0	0
6	*cis*-2-Hexene	93	100	80[f]	*cis*-Epoxide	450	820	640
					trans-Epoxide	40	30	20
					SR/*RS*-Diol	280	10	10
					RR/*SS*-Diol	10	0	0
7	*cis*-Stilbene	82	77	32	*cis*-Epoxide	260	260	110
					trans-Epoxide	200	160	150
					meso-Hydrobenzoin	40	30	10
					Hydrobenzoin	40	20	10
8	Styrene	97	100	44	Epoxide	860	860	380
					Ph(CH)(OH)CH_2OH	60	50	0
					PhC(O)CH_2OH	10	30	0

[a] Co-catalyst GMHA (25 mol%).

[b] Co-catalyst mixture of GMHA (25 mol%) and oxalate (0.3 mol%).

[c] Co-catalyst oxalate (0.3 mol%), for similar experiments with a larger excess of H_2O_2, see Ref. 8a.

[d] All products were identical to independent samples and identified by GC and ^{1}H NMR.

[e] Determined by GC.

[f] 32 mmol scale

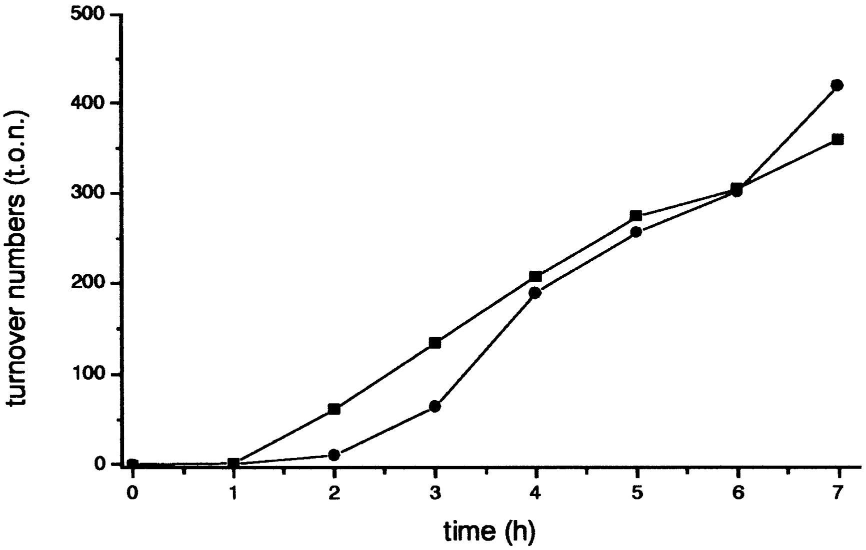
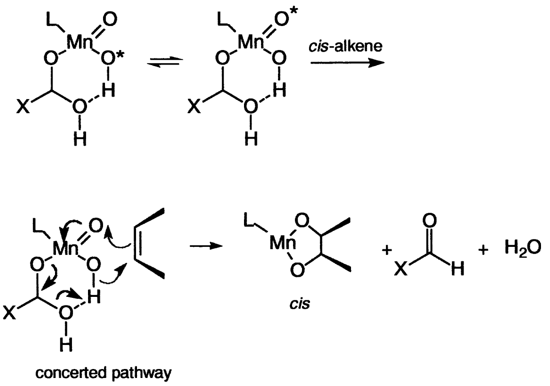


Figure 2. Time profile of the oxidation of cyclooctene by H_2O_2 with catalyst 1 and GMHA; ■ epoxide; ● *cis*-diol.

ide, thus excluding epoxide hydrolysis.[13] This conclusion is further supported by the time course profile of the **1**/GMHA-catalysed oxidation of cyclooctene, which shows that both epoxide and diol increase progressively with time (Fig. 2).

Attempts to increase the *cis*-diol selectivity by addition of acid or base resulted in a dramatic decrease of conversion. Besides GMHA, a few other carbonyl compounds were tested as co-catalyst (25 mol%) for the oxidation of cyclooctene with H_2O_2 (1.3 equiv.). In the presence of glyoxylic acid hydrate, the epoxide was formed in 840 t.o.n. and *cis*-diol formation was almost completely suppressed. Modest *cis*-diol yields (<250 t.o.n.) and predominant formation of the epoxide were seen with diethyl ketomalonate or 2-ketoglutaric acid as the co-catalysts. However, *cis*-diol formation (370 t.o.n.) predominated over epoxide (310 t.o.n.) formation in the presence of chloral hydrate. Thus, a variety of carbonyl compounds with an adjacent electron withdrawing group are able to reduce H_2O_2 decomposition by **1** and to impose *cis*-dihydroxylation activity on manganese catalyst **1**, albeit with variable *cis*-diol/epoxide ratios.

Since *cis*-diol formation through Mn-catalysed epoxide hydrolysis can be excluded (vide supra), we propose that the *cis*-diol is formed by reaction of the alkene with an Mn oxo-hydroxo species. As in the case of oxalate, hydrated activated carbonyl compounds[14] might break down the catalase active binuclear Mn complex **1**[15] into a mononuclear Mn species via complexation to the Mn centre. *cis*-Diol formation from an Mn oxo-hydroxo species with a coordinated hydrated carbonyl ligand could be induced through a hydrogen bonded six-membered ring transition state (concerted pathway, Scheme 1). Reoxidation of the Mn centre with H_2O_2, release of the diol from Mn, and hydration of the carbonyl compound closes the catalytic cycle. In conclusion, use of activated carbonyl compounds in combination with Mn–tmtacn results in a highly active (up to 860 t.o.n.) and H_2O_2 efficient epoxidation system. Besides epoxidation this new catalytic system also provides, to the best of our knowledge, the most active Os-free homogeneous catalyst for *cis*-dihydroxylation (up to 420 t.o.n.). Compared with the anchored Mn–tacn catalyst,[9] the present homogeneous **1**/activated carbonyl compound system is much more accessible, since both **1** and many activated carbonyl compounds have large scale applications. Efforts to enhance diol selectivity and to elucidate the *cis*-dihydroxylation mechanism are in progress.



Scheme 1. Proposed *cis*-dihydroxylation mechanism (L = tmtacn, X = CO_2Me, CCl_3).

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11. Typical oxidation procedure with Mn–tmtacn/GMHA system: H_2O_2 (50% aq., 52 mmol) was added in 6 h at 0°C to a solution of $Mn_2O_3(tmtacn)_2(PF_6)_2$ (**1**, 0.04 mmol), GMHA (10 mmol), substrate (40 mmol) and internal standard (1.2-dichlorobenzene, 20 mmol) in acetonitrile (40 mL). Samples for GC (HP 6890, column HP1 15×0.3 mm×2.65 μm, polymethylsiloxane) analysis were taken 1 h after complete addition of oxidant.
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