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cis-Dihydroxylation and Epoxidation of Alkenes by $[Mn_2O(RCO_2)_2(tmtacn)_2]$: Tailoring the Selectivity of a Highly H_2O_2-Efficient Catalyst

Johannes W. de Boer,[†] Jelle Brinksma,[†,‡] Wesley R. Browne,[†] Auke Meetsma,[†] Paul L. Alsters,[§] Ronald Hage,[⊥] and Ben L. Feringa*,[†]

Department of Organic and Molecular Inorganic Chemistry, Stratingh Institute, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands, Kiadis B.V., Zernikepark 6-8, 9747 AN Groningen, The Netherlands, DSM Pharma Chemicals, Advanced Synthesis, Catalysis and Development, P.O. Box 18, 6160 MD Geleen, The Netherlands, and Unilever R&D Vlaardingen, P.O. Box 114, 3130 AC Vlaardingen, The Netherlands

Received February 16, 2005; E-mail: b.l.feringa@ rug.nl

cis-Dihydroxylation and epoxidation of alkenes are key chemical transformations in synthetic organic chemistry,[1] for which both stoichiometric oxidants (e.g., peracids, MnO_4^-, OsO_4)[2] and second- and third-row transition metal-based oxidation catalysts[3] have proven to be very effective. In recent years, considerable advances have been made in the development of atom-efficient and environmentally friendly catalytic methods employing H_2O_2,[1] most notably in the use of Mn^{II} salts[4] and Fe^{II} complexes[5,6] in the catalytic epoxidation of alkenes. In contrast, first-row transition metal-catalyzed cis-dihydroxylation of alkenes remains a considerable challenge. Nevertheless, the recent report by De Vos et al. with heterogenized Mn-tmtacn,[7] Que et al. with Fe^{II} pyridyl-amine-based complexes,[5] and our results[8] on the use of the oxidation catalyst $[Mn^{IV}_2O_3(tmtacn)_2]^{2+}$ (**1**),[9,10] in the presence of electron deficient aldehydes, demonstrate the potential of these metals toward cis-dihydroxylation.

We describe here the carboxylic acid-promoted cis-dihydroxylation and epoxidation of alkenes catalyzed by **1** employing H_2O_2 as oxidant. The use of carboxylic acids at cocatalytic levels (Table 1, entries 1−3 and 7−10) not only is effective in suppressing the inherent catalase activity of **1**,[11] but also enables the tuning of the catalyst's selectivity toward cis-dihydroxylation and epoxidation. Spectroscopic studies and X-ray analysis[12] confirm that the control arises from the in situ formation of carboxylate-bridged dinuclear complexes, for example, complex **2** $\{[Mn^{III}_2O(CCl_3CO_2)_2(tmtacn)_2]^{2+}\}$ and complex **3** $\{[Mn^{II}_2(OH)(CCl_3CO_2)_2(tmtacn)_2]^{+}\}$, during catalysis (Figure 1).

Preliminary experiments employing **1** (0.1 mol %) and CCl_3CO_2H demonstrated improved activity toward the oxidation of alkenes compared with the electron-deficient aldehydes reported earlier,[8] albeit with slightly reduced selectivity toward the *cis*-diol (entries 12 and 13). In stark contrast, however, the use of carboxylic acids at lower (cocatalytic) concentrations (2−10 equiv wrt **1**, entries 1 and 2) resulted in an increase in selectivity toward cis-dihydroxylation.[13] A significant decrease in activity was observed only at <0.2 mol % CCl_3CO_2H (less than two carboxylate ligands wrt **1**, entries 2−5). This acid concentration dependence suggests that the active catalyst contains two $CCl_3CO_2^-$ ligands. The activity of **2** in the absence of CCl_3CO_2H (entries 2−6) supports this conclusion.

A lag time (∼1 h) is observed in the oxidation of cyclooctene catalyzed by **1**/CCl_3CO_2H (entry 1 and Figure 2). Spectroscopic analysis (UV−vis and ESI-MS)[12] confirms that **2** forms quantitatively during the lag phase via a net two-electron reduction of **1** by H_2O_2 and exchange[14] of two μ-O ligands with two carboxylates. This confirms that **1** is not the active catalyst and that **2** is either the immediate precursor of the catalytically active species and acts as a "catalyst reservoir" during the reaction or is the resting state of the catalyst during the catalytic cycle. Indeed, the spectroscopic properties and activity observed during the cyclooctene oxidation

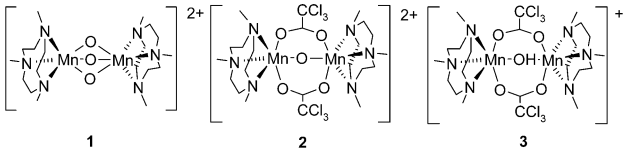

Figure 1. Structures of complexes **1**, **2**, and **3**.

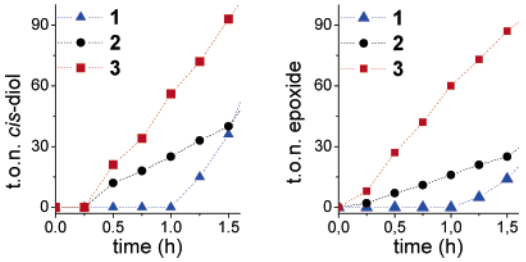

Figure 2. Product formation (0−1.5 h) for reaction with **1**, **2**, and **3** (1.0 mol % CCl_3CO_2H; see Table 1, entries 1, 7, and 8) with cyclooctene. See Figure S1 for complete (7 h) time trace.

Table 1. Oxidation of Cyclooctene to *cis*-Diol and Epoxide[a]

entry	catalyst/cocatalyst (mol %)	conv %[b]	T.O.N.[c] *cis*-diol	epoxide
1	**1**/CCl_3CO_2H (1.0)	91	440	245
2	**1**/CCl_3CO_2H (0.2)	59	340	145
3	**1**/CCl_3CO_2H (0.1)	9	65	25
4	**1**/−	3	10	5
5	**1**/HPF_6 (1.0)	3	10	20
6	**2**/−	44	270	110
7	**2**/CCl_3CO_2H (1.0)	93	380	260
8	**3**/CCl_3CO_2H (1.0)	90	380	280
9	**1**/2,6-Cl_2PhCO_2H (3.0)	67[d]	525	75
10	**1**/salicylic acid (1.0)	82	60	695
11	**1**/chloral hydrate (1.0)	3	20	15
12	**1**/CCl_3CO_2H (25)	96	325	405
13	**1**/chloral hydrate (25)[e]	88	370	310

[a] Reaction conditions: **1**/cyclooctene/H_2O_2 1/1000/1300, H_2O_2 added over 6 h, reported data after 7 h, general procedure A. All values within 10%. [b] wrt substrate consumed. [c] For details of other oxidation products, see ref 12. [d] Isolated yield *cis*-cyclooctane-1,2-diol: 46%. [e] Reference 8.

[†] University of Groningen.
[‡] Kiadis B.V.
[§] DSM Pharma Chemicals.
[⊥] Unilever R&D Vlaardingen.

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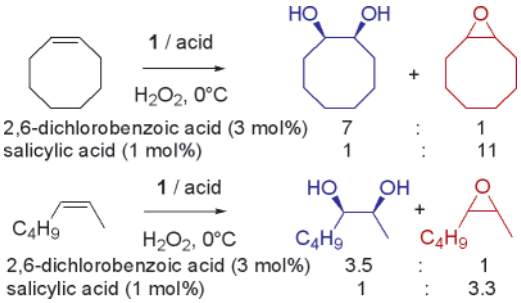
Scheme 1



catalyzed by complex **2** (Mn^{III}_2) or **3** (Mn^{II}_2) (entries 7 and 8) were remarkably similar to that of the parent "**1**/CCl_3CO_2H" system (entry 1).[12]

Overall, only a very modest effect of the catalyst employed (i.e., **1**, **2**, or **3**) on reactivity and selectivity was observed (entries 1, 7, and 8). In contrast, the effect observed on the lag time and selectivity during the initial phase of the reaction is striking (Figure 2). For both **2** and **3**, a significant reduction in the lag time is observed together with a reduced selectivity toward cis-dihydroxylation (until ~90 min) compared with **1**. Moreover, a distinct difference in the reactivity of **2** and **3** during the first ~90 min of the reaction was observed, after which all three complexes exhibit similar kinetics and almost identical spectroscopic features.[12] The results indicate that the reaction involves low-valent dinuclear Mn complexes (e.g., **2** and **3**).

Identification of the involvement of $CCl_3CO_2^-$ as a ligand in the catalytically active species implied that both the selectivity and reactivity may be tunable. This prompted a screening program of more than 30 substituted alkanoic and benzoic acids, which led to the identification of more selective cocatalysts than CCl_3CO_2H toward the cis-dihydroxylation or epoxidation of cyclooctene, that is, 2,6-dichlorobenzoic acid and salicylic acid (entries 9 and 10 and Scheme 1). As for CCl_3CO_2H, for both 2,6-dichlorobenzoic and salicylic acid carboxylate complexes are formed during the lag period, indicating that the differences in selectivity and reactivity observed can be related directly to the nature of the ligating carboxylate and not to nonspecific pH effects.[12] The role of the proximal hydroxyl group of the salicylate as a hydrogen bonding or proton source may be key to the increased epoxide selectivity.

Together with CCl_3CO_2H, these two acids were employed in the oxidation of a series of alkenes representing key structural classes (Table S2). As for cyclooctene, for *cis*-2-heptene either the *cis*-diol or the *cis*-epoxide is obtained as the major product using 2,6-dichlorobenzoic or salicylic acid, respectively (Scheme 1). Furthermore, retention of configuration (RC)[12] for both the *cis*-diol (RC > 96%) and epoxide (RC > 95%) is observed, indicating that the reaction between the alkene and the activated catalyst proceeds via a concerted pathway.[5] While high conversion is achieved with electron-rich alkenes, electron-deficient alkenes (i.e., dimethyl maleate and dimethyl fumarate) give only low reactivity, indicating that the catalyst is electrophilic in nature.

The very high activity of the present system was found to be its Achilles' heel as exemplified in the oxidation of several of the substrates (e.g., 1-octene, cyclohexene[12]). In contrast to electron-deficient alkenes (vide supra), the reduced yields of *cis*-diol and epoxide with several of these substrates are not due to low catalyst activity. Indeed high conversions (70−90% based on substrate) were observed in almost all cases (Table S2). There are two possible explanations for this behavior: further oxidation of the *cis*-diol formed and/or the involvement of competing oxidation processes other than cis-dihydroxylation and epoxidation (e.g., C−H bond activation and/or allylic oxidation).[15] For cyclooctene, in the later stages of the reaction, the low alkene concentration results in oxidation of the *cis*-diol as a competitive process, and continued addition of excess H_2O_2 leads to complete oxidation of the *cis*-diol formed initially. Maintaining cyclooctene concentration at pseudo-steady-state levels, however, suppresses overoxidation (Figure S5) and allows for up to 2000 turnover numbers (TONs) for *cis*-diol.[12] For other substrates, this approach also resulted in an increased yield of *cis*-diol and epoxide.[12]

In summary, carboxylic acids as cocatalysts allow for both the suppression of catalase activity and, through the formation of carboxylate-bridged dinuclear Mn complexes, control over the selectivity and activity toward cis-dihydroxylation and epoxidation. To the best of our knowledge, the system **1**/2,6-dichlorobenzoic acid (2000 TONs for *cis*-cyclooctanediol) is the most active Os-free cis-dihydroxylation catalyst reported to date.

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Supporting Information Available: Analytical, experimental, and X-ray data for **2** and **3**. Mass and UV−vis spectral data. Catalytic protocols (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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