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Highly Efficient Isobutyraldehyde-Mediated Epoxidation of Cyclic Alkenes with Dioxygen Catalyzed by a Novel Dimeric Manganese(II) Complex Containing an Easy-to-Prepare Flexible Carboxamide Ligand

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Dioxygen epoxidation of cyclic alkenes into their corresponding epoxides was successfully achieved in good yield by using a novel binuclear manganese carboxamide complex as the catalyst and isobutyraldehyde as the cosubstrate.

Selective oxidation of alkenes using molecular oxygen is one of the most important challenging transformations in the synthesis of fine chemicals because of the low cost and environmentally friendly nature of the oxidant.[1] However, it is difficult to control the reaction because of overoxidations or side reactions under conventional severe reaction conditions, such as the high pressure of oxygen or high reaction temperature. Thus, it is desired to search for milder reaction conditions to suppress these reactions for the development of an efficient epoxidation method. Mukaiyama and co-workers[2] and others[3] have reported that molecular oxygen can be used as the terminal oxidant in the epoxidation of alkenes with an aldehyde or primary alcohol as the coreactant and a metal β-diketonate as the catalyst. Under mild conditions, epoxidation of cyclohexene, 1-phenylcyclohexene, and 1-methylcyclohexene gave the corresponding epoxides in 84.5, 84.6, and 93.4% yield, respectively, by using a manganese carboxamide complex.[4] In Thomas and co-worker's report, the corresponding epoxides are produced in moderate yields by using manganese(III)- and cobalt(III)-containing molecular sieves with a reaction time of 8 h in 50 °C.[5] Corain et al. described a selective epoxidation of cyclohexene by using copper β-carbonylenolate and obtained higher selectivity after 20−30 h.[6] On the other hand, the past 2 decades have seen considerable interest in manganese redox enzymes, particularly those containing binuclear active sites,[7] such as manganese ribonucleotide reductase, which catalyzes the O_2-dependent reduction of ribonucleotides to deoxyribonucleotides.[8] According to the limiting crystallographic data for the native manganese enzymes, studies concerning the reactivity of manganese model complexes bearing some structural features similar to those proposed for the different forms of the enzymes can help in the understanding of the mechanism of enzyme activation.

In this Communication, we report on the synthesis and molecular and crystal structure characterization of a new dimeric manganese(II) complex, $[Mn_2(HL)_2Cl_4(CH_3OH)_2]$ (**1**), where HL is *N*-(2-pyridylmerhyl)-2-pyrazinecarboxamide. We also studied the catalytic activity of **1** toward the epoxidation of cyclic alkenes in the presence of O_2 (oxidant) and isobutyraldehyde (cosubstrate) under mild reaction conditions. The catalytic activity of **1** in the epoxidation of cyclic alkenes that are summarized in Tables 1 and 2 shows excellent conversion and selectivity.

The ligand used in this study (Scheme 1) was prepared using strategy reported previously.[9] The manganese

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Table 1. O_2 Epoxidation of Cyclohexene Using **1** as the Catalyst[a]

entry	t (h)/T (°C)	catalyst (mmol)	aldehyde (mmol)	convn (%)	epoxide selectivity (%)[b]
1	1/60	1.76×10^{-3}	1.76	24.0	94.0
2	3/60	1.76×10^{-3}	1.76	64.0	93.0
3	3/60	3.52×10^{-3}	1.76	75.0	93.8
4	3/60	7.04×10^{-3}	1.76	88.3	95.0
5	6/0	1.76×10^{-3}	1.76	54.8	96.5
6	6/30	1.76×10^{-3}	1.76	83.0	95.7
7	6/60	1.76×10^{-3}	1.76	>99.9	97.6
8	6/60	1.76×10^{-3}	0.88	94.0	97.0
9	6/60	1.76×10^{-3}	0.84	90.0	95.3
10	6/60	−	1.76	21.0	83.0
11	6/60	1.76×10^{-3}	−	4.0	23.0[c]
12	6/60	6.40×10^{-3} ($MnCl_2$)	1.76	37.0	79.2
13	6/60	6.40×10^{-3} (free ligand)	1.76	17.8	84.0
14[d]	6/60	1.76×10^{-3}	1.76	3.0	17.0

[a] Reaction condition: substrate (0.88 mmol), catalyst (1.76×10^{-3} mmol), isobutyraldehyde (1.76 mmol), and O_2 (1 atm) in 2 mL of a dimethylformamide solvent. [b] By gas/liquid chromatography determination based on internal standards and using authentic samples for comparison. [c] The main byproduct was 2-cyclohexen-1-one (from GC−MS analysis). [d] With 6.40×10^{-3} mmol of 2,6 -di-*tert*-butyl-4-methylphenol as the radical trapping compound.

Table 2. O_2 Epoxidation of Cyclic Alkenes Using **1** as the Catalyst[a]

			selectivity (%)	
entry	substrate	convn (%)	epoxide[b]	others
1	1-methylcyclohexene	>99.9	95.0	5.0
2	1-phenylcyclohexene	>99.9	84.0	16.0
3	cyclopentene	>99.9	96.6	3.3
4	cycloheptene	>99.9	90.0	10.0
5	cyclooctene	99.9	99.2	<1.0

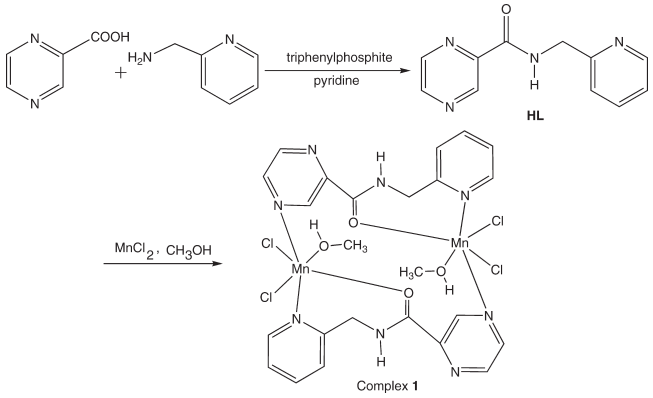
[a] Reaction condition: substrate (0.88 mmol), catalyst (1.76×10^{-3} mmol), isobutyraldehyde (1.76 mmol), and O_2 (1 atm) in 2 mL of a dimethylformamide solvent, 60 °C, reaction time 6 h. [b] By gas/liquid chromatography determination based on internal standards and using authentic samples for comparison.

(II) complex **1** was synthesized by mixing equimolar quantities of $MnCl_2$ and HL in methanol. Compound **1** was isolated as yellow crystals after slow evaporation of methanol for 3 weeks (68% yield; Scheme 1).

The structure of **1** was characterized by Fourier transform IR and elemental analysis and determined by a single-crystal X-ray diffraction method,[10] and the ORTEP diagram is shown in Figure 1.

The structure of **1** consists of a centrosymmetric binuclear manganese complex. The ligand HL binds as a bridging tricoordinating ligand, and the Mn center resides in a distorted octahedral geometry. The coordination sphere of the Mn ion is formed by one carbonyl O atom of HL, two Cl ions, and one methanol molecule defining the equatorial plane and with the pyridine N atom of HL and pyrazine N atom from another carboxamide ligand coordinated to adjacent Mn ions. These two Mn−N bonds define the axial positions. In fact, within the binuclear unit, a pyrazine N atom from one [$Mn(HL)Cl_2(CH_3OH)$] moiety is axially bound to the Mn atom from the other moiety. The Mn1···Mn1#A [#A, $1 - X, -Y + 1, -Z$] intermolecular separation through this unique 12-membered metallacyclic ring in **1** is 7.384(2) Å. The cavity size is measured by the Mn···Mn distance [7.384(2) Å] and the distance between C8···C8#A [#A, $1 - X, -Y + 1, -Z$] atoms [5.257(3) Å]. The cyclic units of [$Mn_2(HL)_2Cl_4(CH_3OH)_2$] are linked by hydrogen bonds between amide N−H and a coordinating chloride along the crystallographic *c* direction (Figure 2a). The average distance between two cyclic units is 5.254 Å. Again, the cyclic units involved intermolecular hydrogen bonds between methanolic O−H and the second coordinated chloride anion (Figure 2b). As a result, these two intermolecular hydrogen bonds led to the close-packed structure in such a way that infinite chains of adjacent cyclic units connected together by O−H···Cl hydrogen bonds produce channels parallel to the crystallographic *b* axis and each channel is connected to the adjacent channel by N−H···Cl hydrogen bonds (Figure 2c).

Scheme 1. Synthetic Route of Ligand HL and the Corresponding Manganese Dimeric Complex **1**



This binuclear manganese complex is found to be highly active and remarkably selective in the epoxidation of cyclic alkenes at room temperature using O_2 as the oxidant and isobutyraldehyde as the cosubstrate, a reaction of high scientific and commercial interest. In the oxidation of cyclohexene with O_2, we found that increased catalyst loading from 1.76×10^{-3} to 7.04×10^{-3} mmol increases conversion from 64.0% to 88.3% (Table 1, entries 2−4).

When the catalyst-to-substrate molar ratio was 0.002, isobutyraldehyde had a notable effect on the epoxidation of cyclohexene, and with a decrease of the concentration of isobutyraldehyde from 1.76 to 0.84 mmol, the conversion

(10) Crystal data for **1**: $C_{24}H_{24}Cl_8Mn_2N_8O_4$ (M_r = 744.22), monoclinic, space group $P2_1/n$, a = 12.7836(12) Å, b = 6.9523(6) Å, c = 17.2215(16) Å, β = 106.194(7)°, V = 1469.8(2) Å^3, Z = 2, D_{calc} = 1.682 g cm^{-3}, μ = 1.270 mm^{-1}, T= 120(2) K, crystal size 0.32 × 0.31 × 0.30 mm^3, R1 = 0.0250, wR2 = 0.0621, GOF = 1.084 with $I > 2\sigma(I)$. CCDC 717556.

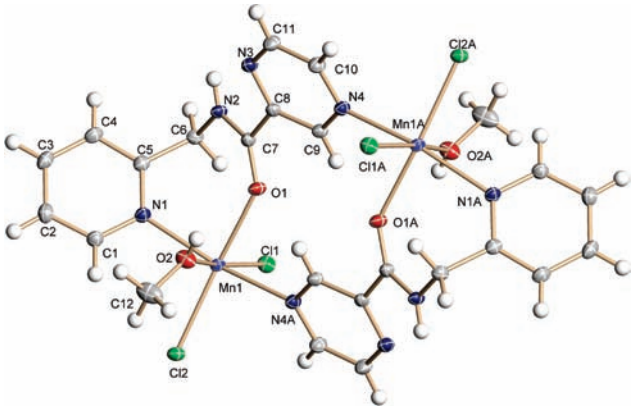


Figure 1. ORTEP diagram of compound **1**. Ellipsoids are drawn at the 50% probability level. Selected bond distances (Å) and angles (deg): Mn1−N1, 2.2966(12); Mn1−N4#A, 2.3199(12); Mn1−O1, 2.2218(11); Mn1−O2, 2.2546(12); Mn1−Cl1, 2.4767(5); Mn1−Cl2, 2.4545(4); Mn1−Mn1#A, 7.384(2); N1−Mn1−N4#A, 165.51(5); N1−Mn1−O1, 88.45(4); N1−Mn1−O2, 83.98(4); N1−Mn1−Cl1, 101.10(3); N1−Mn1−Cl2, 97.14(3); N4#A−Mn1−O1, 81.03(4); N4#A−Mn1−O2, 84.33(5); N4#A−Mn1−Cl1, 89.34(3); N4#A−Mn1−Cl2, 91.19(3); O1−Mn1−O2, 79.66(4); O1−Mn1−Cl1, 92.33(3); O1−Mn1−Cl2, 166.74(3); O2−Mn1−Cl2, 88.93(3); O2−Mn1−Cl1, 170.47(3); Cl1−Mn1−Cl2, 98.34(2); N2−C6−C5, 112.45(12); C1−N1−Mn1−N4#A, −98.53(19); C1−N1−Mn1−O1, −141.86(11); C1−N1−Mn1−O2, −62.09(11); C1−N1−Mn1−Cl1, 126.06(10); C1−N1−Mn1−Cl2, 26.07(11) [#A, 1 − *X*, −*Y* + 1, −*Z*].

decreased from >99.9% to 90.0% (Table 1, entries 7−9) as expected. In the absence of isobutyraldehyde (Table 1, entry 11), a low conversion rate and low selectivity were observed and the main byproduct was 2-cyclohexen-1-one [from gas chromatography−mass spectrometry (GC−MS) analysis]. On the other hand, cooxidation of cyclohexene and isobutyraldehyde in the absence of the manganese complex (Table 1, entry 10), in the presence of $MnCl_2$ salt (Table 1, entry 12), or in the presence of a metal-free carboxamide ligand (Table 1, entry 13) furnishes only 21.0, 37.0, or 17.8% conversion of the substrate, respectively, indicating a strong cooperative effect of the manganese complex, isobutyraldehyde, and O_2 under cooxidation conditions.

Although the mechanism of the catalytic reaction is still not clear and the metal catalyst has a complex role,[11a] in order to obtain some information about the reaction mechanism of this oxidation, several parameters have been investigated. No oxidation occurs in the presence of 2,6-di-*tert*-butyl-4-methylphenol as a radical trapping agent (Table 1, entry 14), confirming the free-radical pathway of the reaction. These results are consistent with a reaction mechanism involving free radicals reported by Feiters et al. using porphyrin, cyclam, and β-diketonate complexes of metal as the catalyst.[11] On the other hand, when the reaction temperature was decreased from 60 to 0 °C, the epoxidation rate also decreased (Table 1, entries 5−7).

The scope of the prepared catalyst system was, in turn, tested in the epoxidation of various cyclic olefins

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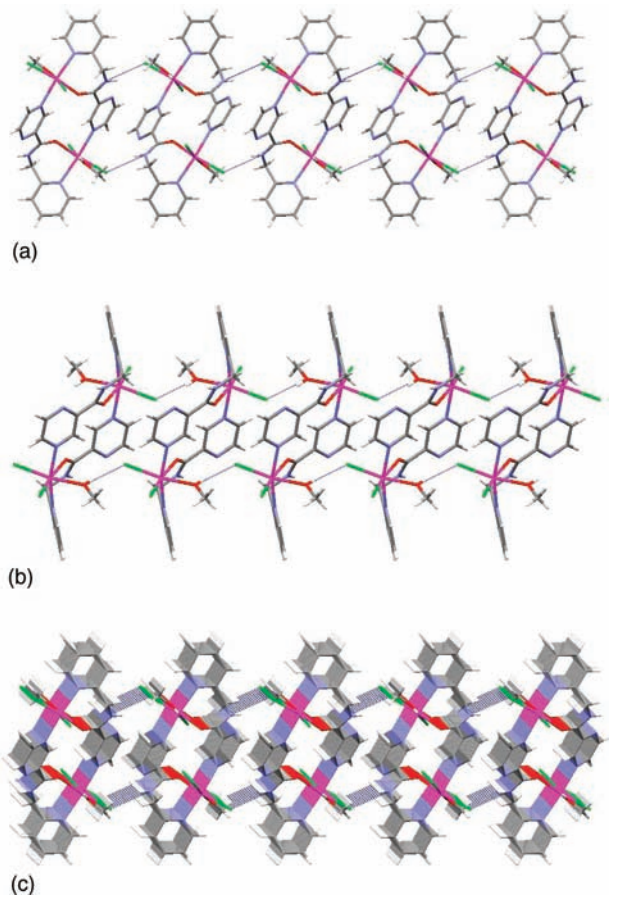

Figure 2. (a) One-dimensional rod-dominant N−H···Cl hydrogen bond motif in the crystallographic *b* direction [H2B···Cl2^{i} = 2.460(2) Å, N2···Cl2^{i} = 3.189(1) Å, and N2−H2B···Cl2^{i} = 147.0(2)°, symmetry code (i) X, $^{3}/_{2} - Y$, $-^{1}/_{2} + Z$]. (b) O−H···Cl hydrogen bond motif in the crystallographic *c* direction [H2C···Cl1^{ii} = 2.34(2) Å, O2···Cl1^{ii} = 3.071(1) Å, and O2−H2C···Cl1^{ii} = 169.0(2)°, symmetry code (ii) X, $-1 + Y$, Z]. (c) Side view of the cyclic unit channels showing the hydrogen bonding between adjacent channels. Hydrogen bonds are presented by dotted lines. C atoms are shown in gray, H atoms in white, Cl atoms in green, Mn atoms in violet, N atoms in blue, and O atoms in red.

(Table 2, entries 1−5). It displays excellent activity with >99.9% conversion and high selectivity in all cases tested. The oxidations of cyclooctene and cyclopentene show high selectivity of 99.2% and 96.6%, respectively.

In conclusion, new dimeric manganese(II) complex **1** with a flexible carboxamide ligand was synthesized and characterized by single-crystal X-ray diffraction. The catalytic activity of this complex in the presence of isobutyraldehyde by molecular oxygen as the oxidant in the epoxidation of cyclic olefins was efficiently accomplished under mild conditions.

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Supporting Information Available: Experimental preparation for **1**, general procedure of the oxidation of cyclic olefins by complex **1**, a sample GC chromatogram, tables of crystallographic data, and X-ray crystallographic data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.